TransMedics®

Bringing new life to organ transplantation™

OCS™ Lung System for the Preservation of Donor Lungs for Transplantation

May 17, 2017

TransMedics, Inc.

Gastroenterology-Urology Devices Panel

Introduction

Waleed Hassanein, MD

President and CEO

TransMedics, Inc.

TransMedics is a Clinically Driven Organization

- Origin of OCS Technology: 1995-98 academic cardiothoracic surgery research project

- TransMedics founded in 2000: developed Organ Care System (OCS™) technology to maintain human solid organs in near-physiologic and functioning state to overcome limitations of cold ischemic storage – OCS Lung, Heart & Liver

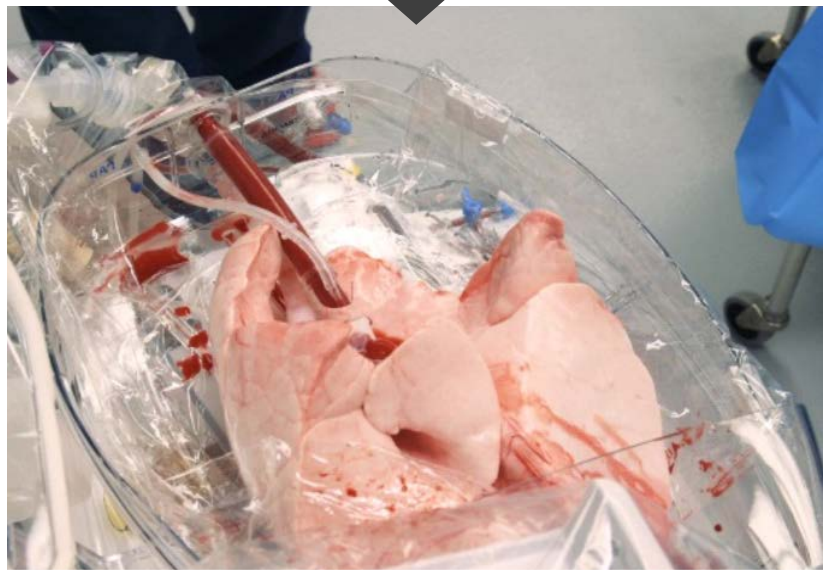
- OCS platform approved outside of U.S. with ~800 successful human transplants performed globally to date in standard, extended, and DCD organ criteria

Establishing High Level of Clinical Evidence – OCS Global Clinical Programs

	LUNG	HEART	LIVER
Standard Criteria	OCS™ Lung **INSPIRE** Trial	OCS™ Heart **PROCEED II** Trial	OCS™ Liver **PROTECT** Trial
Extended Criteria	OCS™ Lung **EXPAND Lung** Trial	OCS™ Heart **EXPAND Heart** Trial	

OCS System Designed to Address Limitations of Cold Ischemic Storage

REDUCE ISCHEMIC INJURY



Warm Oxygenated Blood Perfusion

OPTIMIZE ORGAN CONDITION

Ventilation Recruitment

EX-VIVO FUNCTIONAL ASSESSMENT

Oxygenation, Vascular Resistance, & Airway Compliance

OCS Lung System: Integrated, Portable, Ex-vivo Lung Perfusion and Ventilation System

OCS Lung Console

OCS Lung Perfusion Module

OCS Lung Solution

INSPIRE Demonstrated Assurance of Safety and Effectiveness of OCS Lung System

- Met primary effectiveness and safety endpoints
- Clinically significant reduction in PGD Grade 3 within 72 hours
- Similar safety profile of OCS Lung System to standard of care
- Other clinical benefits that will be further studied in post-market

Proposed Indication for Use

The TransMedics® Organ Care System™ (OCS) Lung System is a portable organ perfusion, ventilation, and monitoring medical device intended to preserve donor lungs in a near physiologic, ventilated, and perfused state for transplantation.

Agenda

Clinical Needs and Current Limitaitons of Cold Storage Preservation	**Gabriel Loor, MD** Associate Professor of Surgery; Director, Lung Transplantation Baylor College of Medicine
Regulatory History	**Waleed Hassanein, MD**
INSPIRE Trial Design	**Abbas Ardehali, MD** Professor of Surgery and Medicine; Chief of Cardiothoracic Transplantation UCLA School of Medicine
INSPIRE Trial Adjudication	**John Wallwork, FRCS, FmedSCI** Emeritus Professor, Cardiothoracic Surgery Papworth Hospital Past President, International Society for Heart and Lung Transplant (ISHLT)
INSPIRE Trial Results	**Gregor Warnecke, MD** Prof. of Surgery; Director of Cardiothoracic Transplantation Hannover Medical School
Training and Post-Market Studies	**Waleed Hassanein, MD**
Benefit-Risk Assessment	**Dirk Van Raemdonck, MD, PhD** Professor of Surgery, University Hospital Leuven Medical Center Co-chair of ISHLT PGD Working Group

Additional Experts

DSMB Chairman	**Joshua Sonett, MD** Professor of Surgery Chief, Thoracic Surgery Columbia University Medical Center
Biostatistics	**Christopher Mullin, MS** Biostatistician 3D Communications, LLC
Device Design and Engineering	**John Sullivan, MS** Vice President, Engineering TransMedics, Inc.
Clinical Operations	**Tamer Khayal, MD** Chief Medical Officer TransMedics, Inc.
Regulatory	**Miriam Provost, PhD** **Christine Brauer, PhD** **Robert Sheridan**

Clinical Needs and Current Limitations of Cold Storage Preservation

Gabriel Loor, MD

Associate Professor, Department of Surgery

Surgical Director of Lung Transplantation

Division of Cardiothoracic Transplantation and Circulatory Support

Michael E. DeBakey Department of Surgery

Baylor College of Medicine

Transplantation is Gold Standard for Treating End-stage Lung Failure

- Without transplant, <50% patients alive in 1-2 years
- Lung transplantation provides:
  - Longer life expectancy
  - Improved functional status
  - Better quality of life

Challenges in Lung Transplant Today

- Organ availability
- Older and sicker patients
- Preservation limitation and transplant logistics
- Primary Graft Dysfunction (PGD)
- Bronchiolitis Obliterans Syndrome (BOS)

No Advancements in Organ Preservation for 30 Years

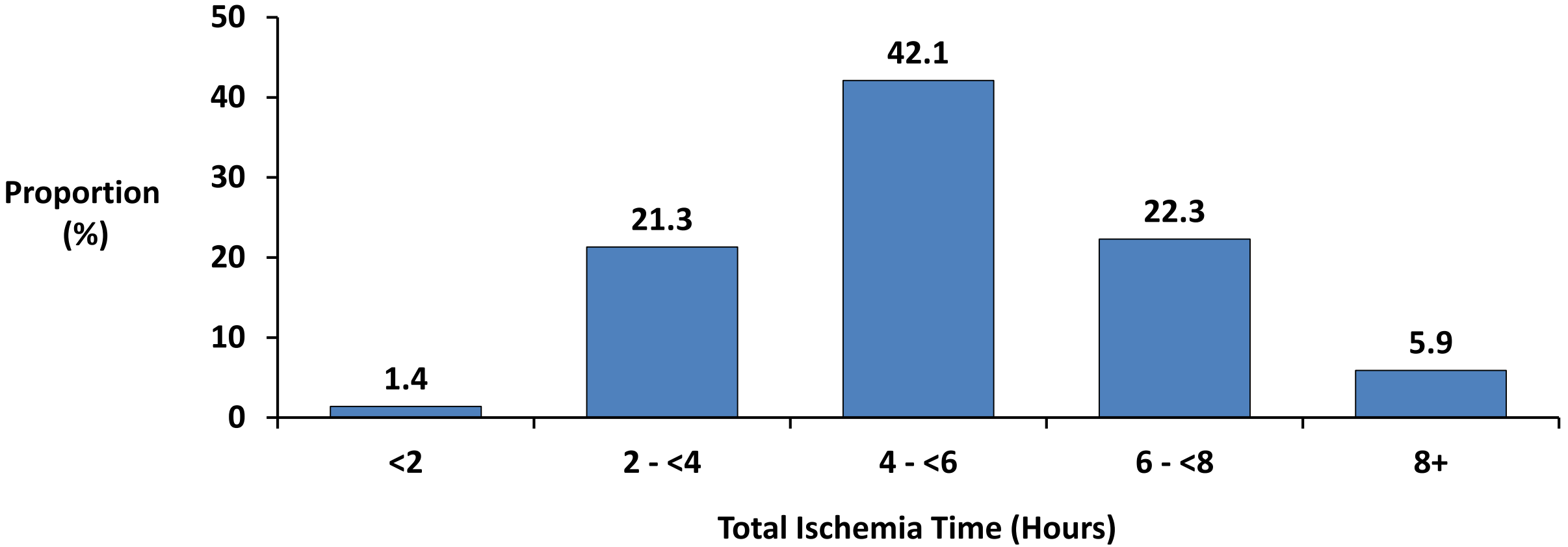
- In last 30 years, many advancements in lung transplantation:
  - Surgical techniques
  - Pre- and peri-operative care of recipients
  - Immunosuppressives
- No advancements in organ preservation beyond cold storage since dawn of organ transplantation

Three Key Limitations of Cold Ischemic Storage

- Time-dependent ischemia / reperfusion injury
- No lung optimization capabilities
- No assessment of lung function

Clinical Constraints of Ischemia in Lung Transplantation

Most U.S. Lung Transplants are <6 Hours



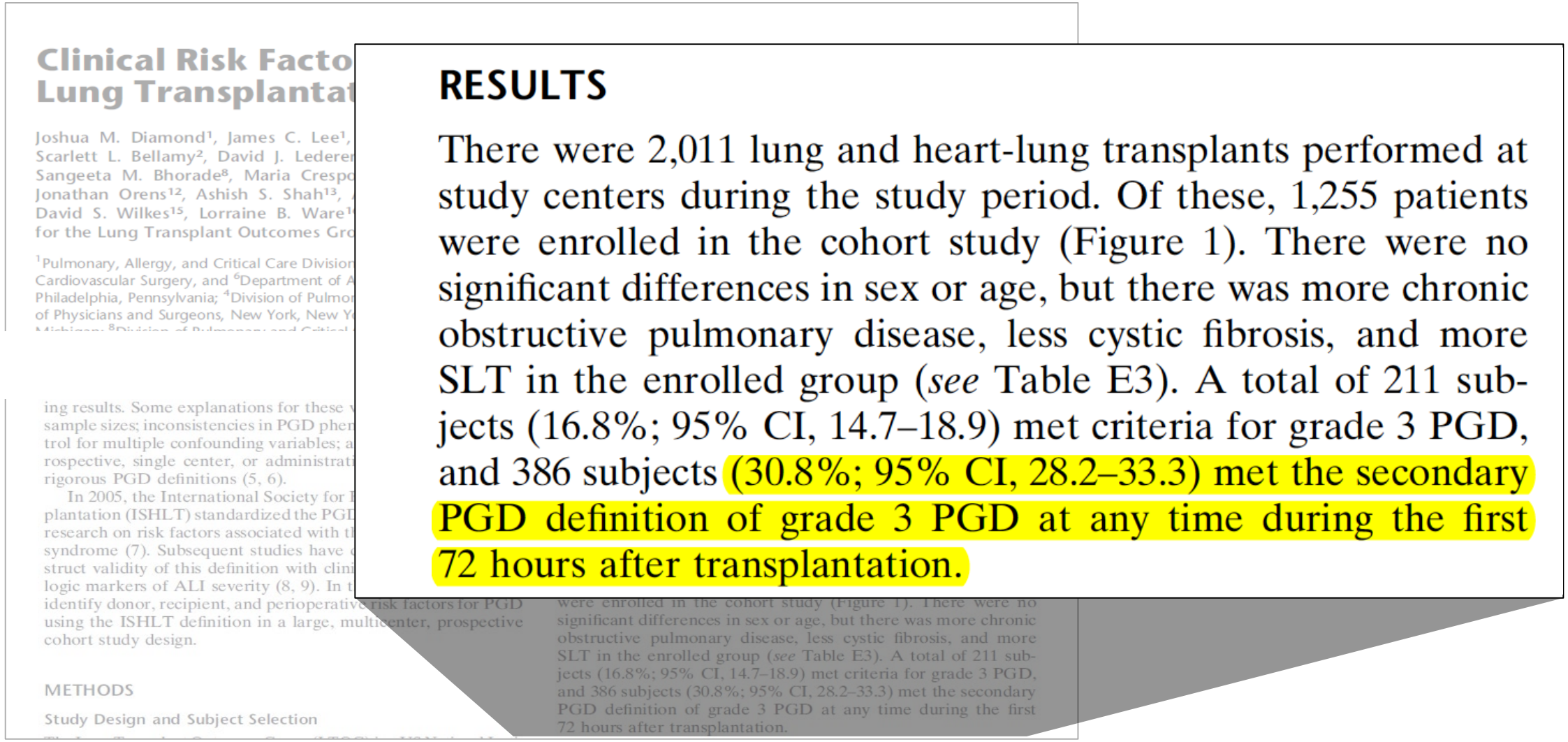
ISHLT Transplant Registry Quarterly Reports for Lung in North America, Jan 2015 – Sep 2016

Primary Graft Dysfunction (PGD) is Acute Lung Injury Associated with Reperfusion Injury

- PGD can occur within first 72 hours after transplant
  - Assessed at T0, 24, 48, and 72 hours post-transplant
- Short-term morbidity associated with PGD
  - Severe hypoxemia, lung edema, difficulty with ventilation, etc.
- ISHLT PGD Grading from 0-3 (0 = absent to 3 = severe)

Diamond JM et al., AJRCCM 2013; 187: 527–534

Reported PGD3 Incidence of 30.8% Within Initial 72 Hours



Clinical Risk Factor
Lung Transplantat

Joshua M. Diamond[1], James C. Lee[1],
Scarlett L. Bellamy[2], David J. Lederer
Sangeeta M. Bhorade[8], Maria Crespo
Jonathan Orens[12], Ashish S. Shah[13],
David S. Wilkes[15], Lorraine B. Ware[1]
for the Lung Transplant Outcomes Gro

[1]Pulmonary, Allergy, and Critical Care Division
Cardiovascular Surgery, and [6]Department of A
Philadelphia, Pennsylvania; [4]Division of Pulmor
of Physicians and Surgeons, New York, New Y

ing results. Some explanations for these
sample sizes; inconsistencies in PGD phen
trol for multiple confounding variables; a
rospective, single center, or administrati
rigorous PGD definitions (5, 6).

In 2005, the International Society for
plantation (ISHLT) standardized the PGD
research on risk factors associated with t
syndrome (7). Subsequent studies have
struct validity of this definition with clini
logic markers of ALI severity (8, 9). In t
identify donor, recipient, and perioperative risk factors for PGD using the ISHLT definition in a large, multicenter, prospective cohort study design.

METHODS

Study Design and Subject Selection

RESULTS

There were 2,011 lung and heart-lung transplants performed at study centers during the study period. Of these, 1,255 patients were enrolled in the cohort study (Figure 1). There were no significant differences in sex or age, but there was more chronic obstructive pulmonary disease, less cystic fibrosis, and more SLT in the enrolled group (*see* Table E3). A total of 211 subjects (16.8%; 95% CI, 14.7–18.9) met criteria for grade 3 PGD, and 386 subjects (30.8%; 95% CI, 28.2–33.3) met the secondary PGD definition of grade 3 PGD at any time during the first 72 hours after transplantation.

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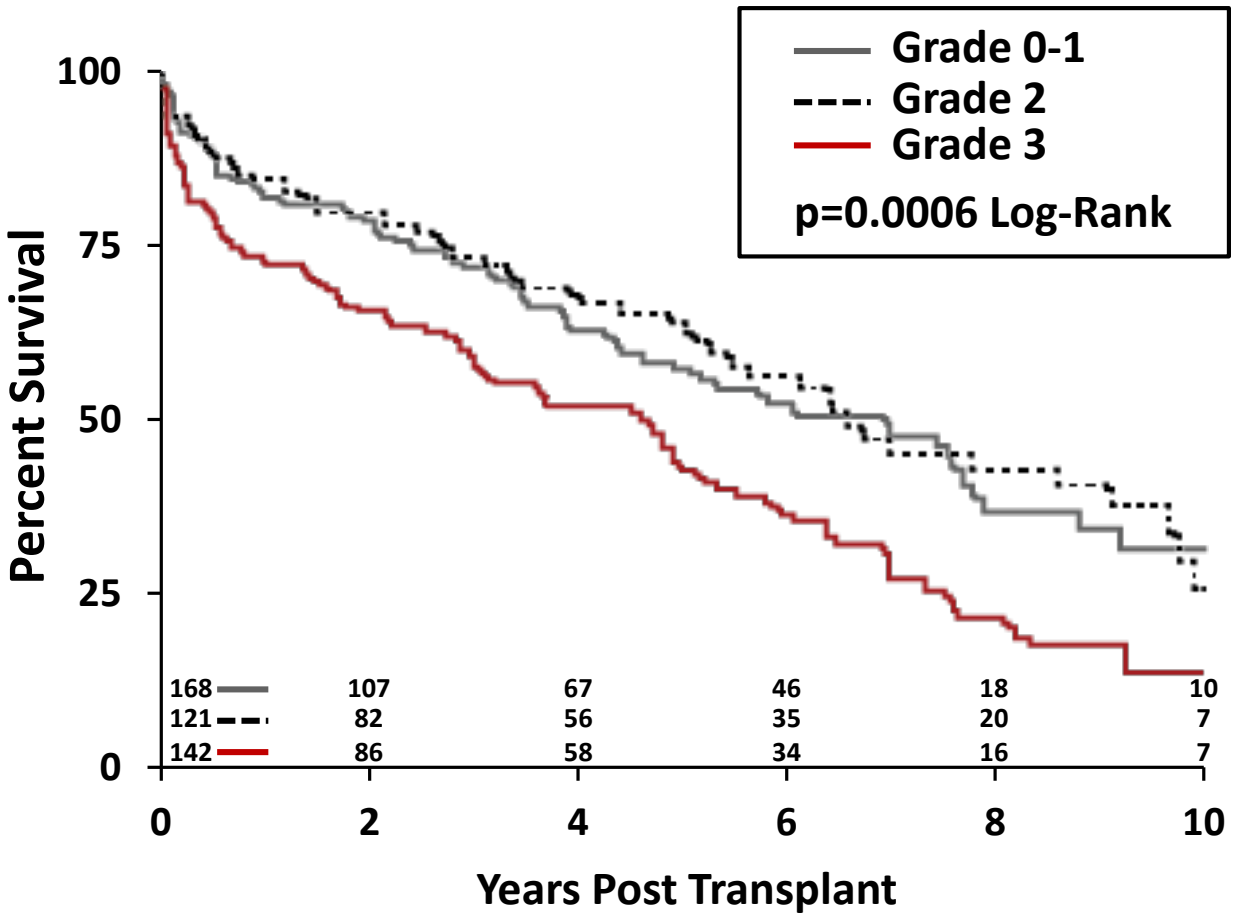
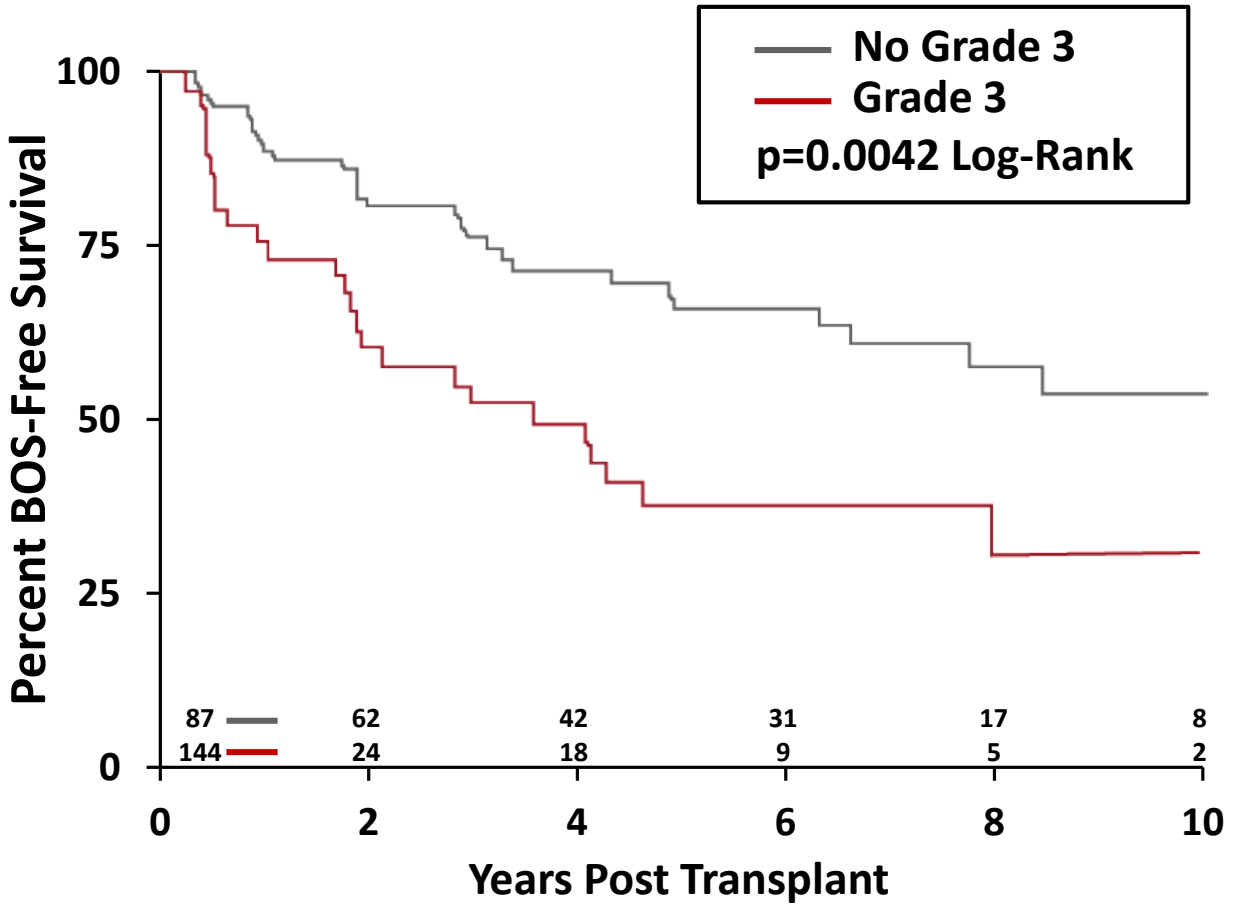
PGD3 Within First 48 Hours Correlates with Lower Long-term Survival, Higher BOS Rate

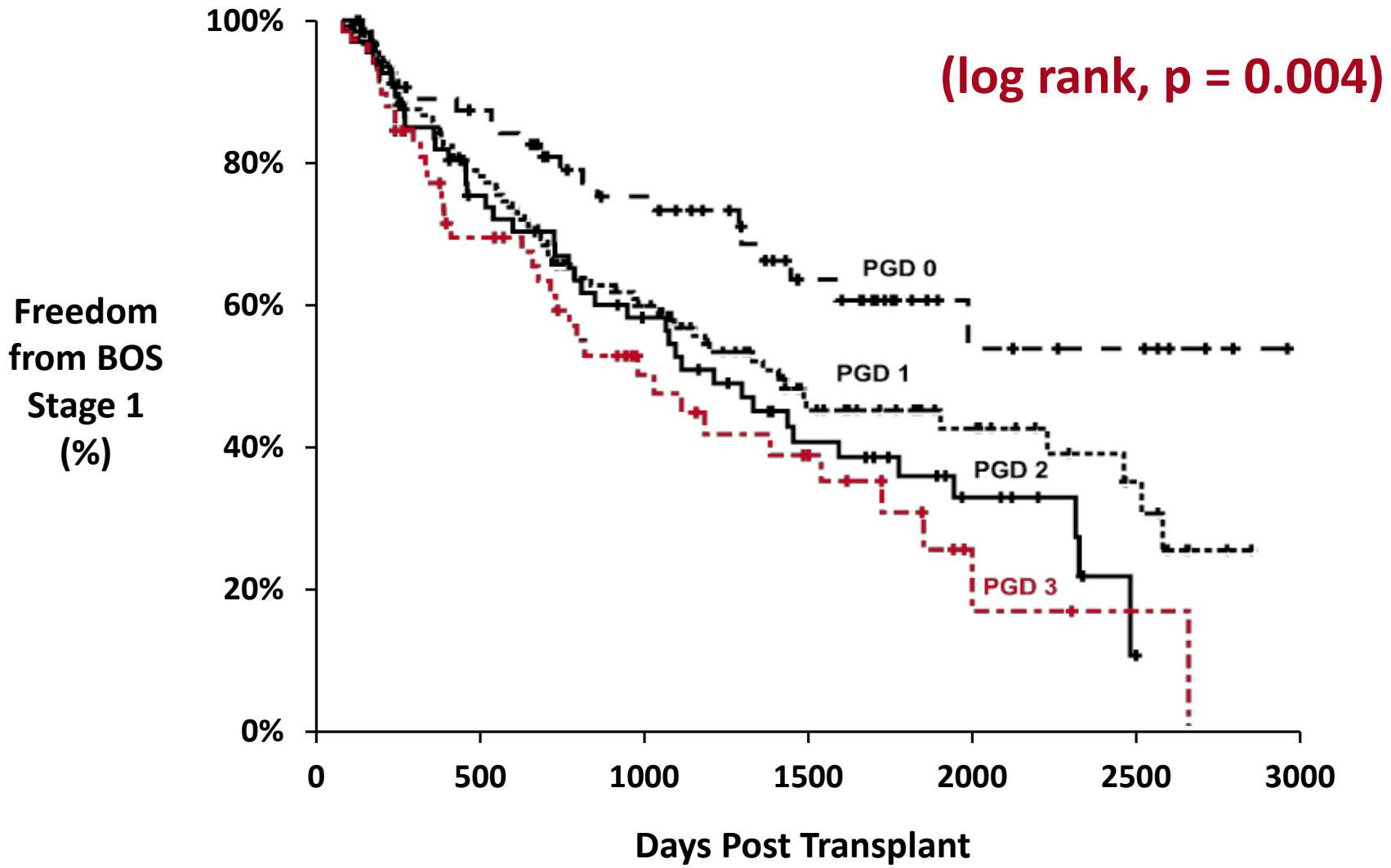




Whitson BA et al., JHLT 2007; 26:1004-1011

FDA Discussion Question 1 & 3

PGD 3 at T0 Correlates with Long-Term BOS Rates

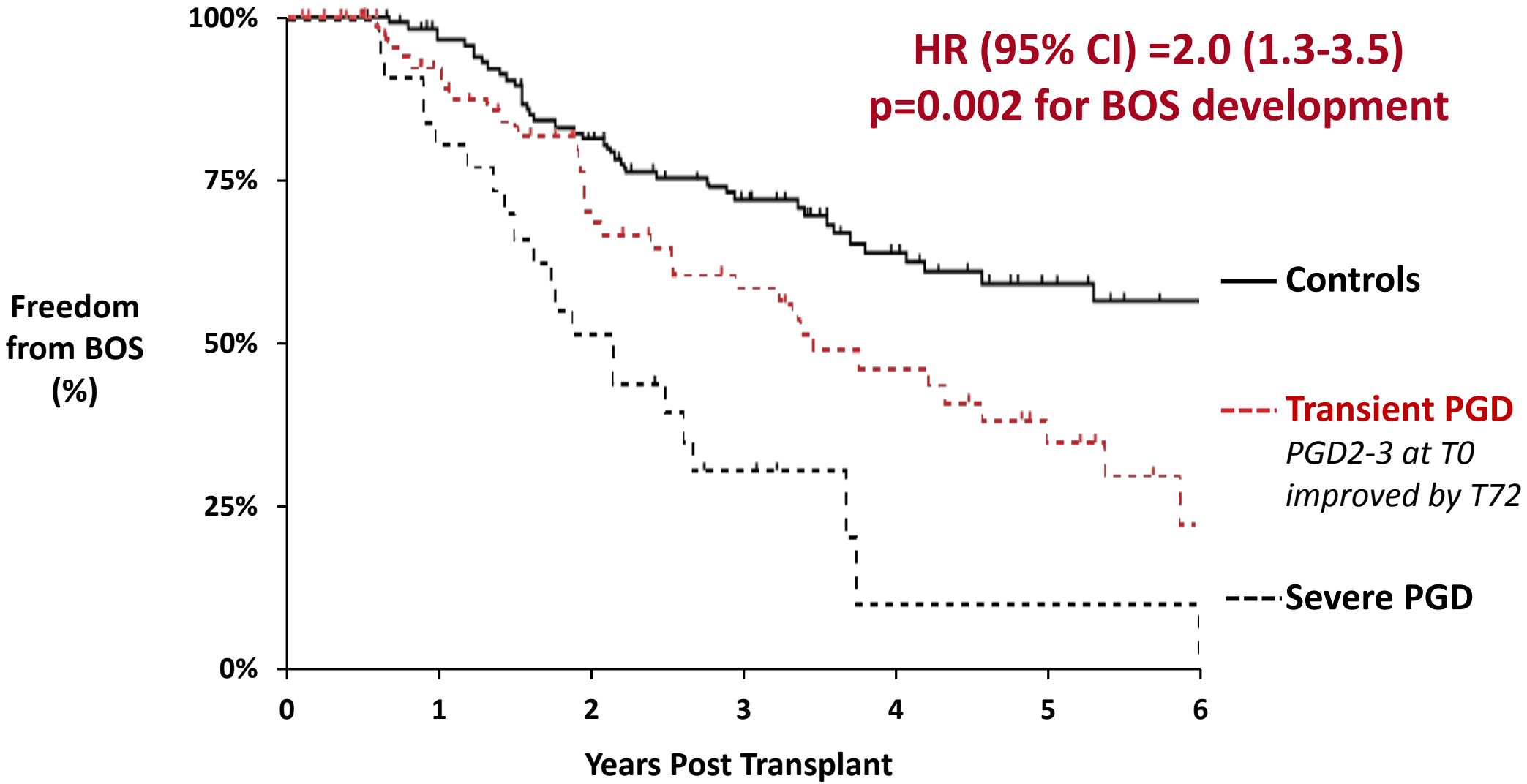


(log rank, p = 0.004)

Daud et al. AMJ. Resp. & Crit. Care Med. 2007

FDA Discussion Question 1 & 3

PGD 2 or 3 at T0 Significant Risk Factor for BOS



DerHovanessian et al, Am J Transplant. 2016; 16(2): 640–649.

FDA Discussion Question 1 & 3

Clinical Need for Advancements in Lung Preservation for Transplantation

- Lung transplantation is gold standard for end-stage lung disease
- Lung preservation limited to cold ischemic storage for past 30+ years with inherent limitations
- PGD3 at any time point within 72 hours associated with poor patient outcomes
- Need for technology to improve lung preservation
  - Minimize ischemic injury
  - Optimize and assess lung during preservation

Regulatory History and Protocol Design of OCS Lung INSPIRE Trial

Waleed Hassanein, MD

President and CEO

TransMedics, Inc.

INSPIRE Trial Regulatory Background

- First RCT for lung preservation for transplantation
- Several challenges to be addressed in study design:
  - Endpoints, analysis population, timing of evaluations, etc.
  - Complex organ allocation and retrieval process

INSPIRE Trial Regulatory Timeline Summary

NOV 2010

IDE Submitted

- 30-day Survival
- PGD3 at T24
- PP population
- NI Margin 10%

DEC 2012

U.S. Trial Initiation

- Composite of 30-day Survival + PGD3 at T72
- mITT population
- NI Margin 4%

DEC 2013

Approved Amendment

- Composite 30-day + PGD3 within T72
- PP population
- PGD3 at T72 secondary
- NI Margin 4%

24 Months of Complex Negotiations

- FDA outlined conditions for IDE approval
- TransMedics agreed to conditions to initiate INSPIRE

EXPAND Lung IDE & ODE Appeal Jan-Dec 2013

Rationale for Protocol Amendment

- Published literature on early PGD
- Successful EXPAND Trial appeal to ODE on scientific merits of PGD3 within 72 hours[1-4]

1. Whitson BA et al., JHLT 2007; 26:1004-1011
2. Daud et al., AMJ. Resp. & Crit. Care Med. 2007
3. Christie J et al., JHLT 2010; 29:2131-2137
4. Huang H et al., AJT 2008: 245402462

Protocol Design Topics for Clarification

Protocol Non-Inferiority Design and Margin

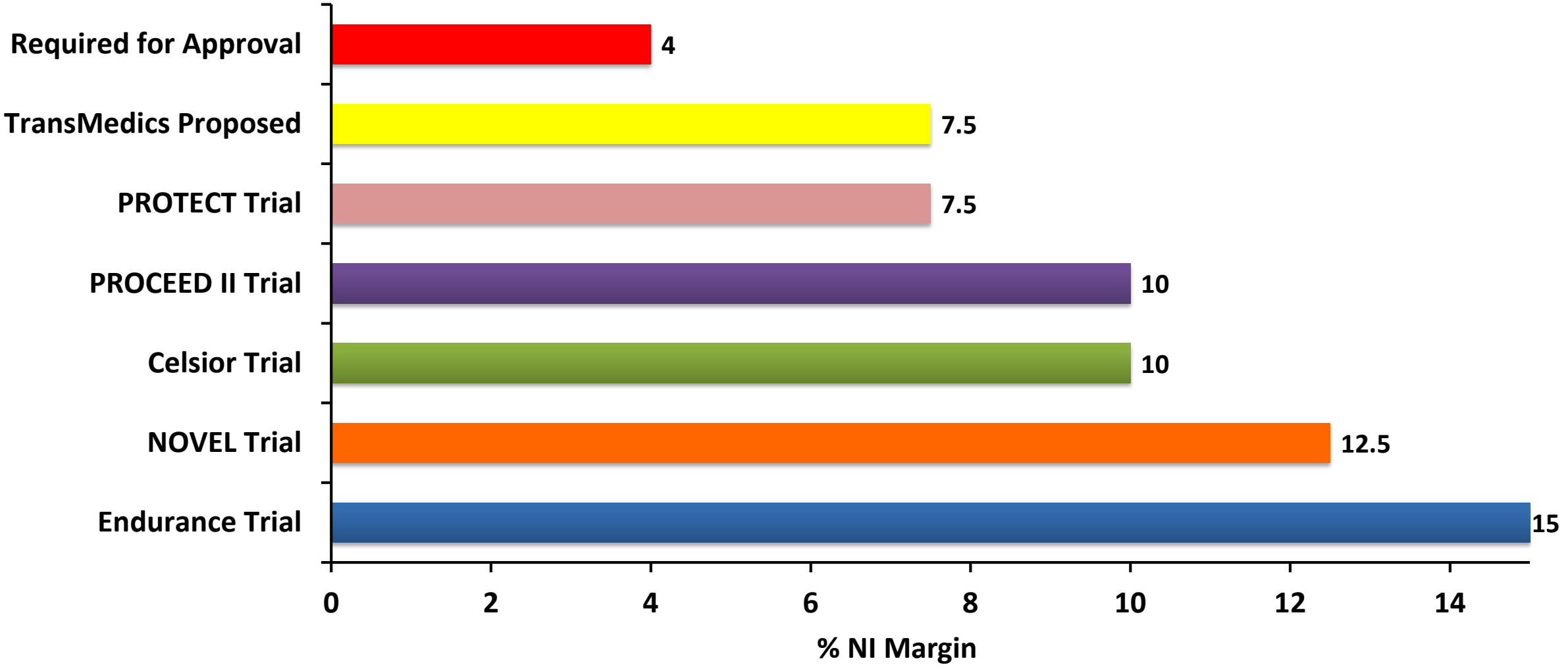
Rationale for Protocol Amendment

Rationale for Administrative Extension Cohort

Non-Inferiority Trial Design

- Rationale for INSPIRE non-inferiority trial design:
  - Very common pivotal FDA trial design for device approval
  - Maintain current success rate of lung transplantation

FDA Required 4% Non-Inferiority Margin



Interpretation of Results with Conservative 4% NI Margin

- To our knowledge, 4% NI margin is narrowest used in pivotal device trial
- OCS had to perform at least 4-5% better than Control to meet NI margin

Protocol Design Topics for Clarification

Protocol Non-Inferiority Design and Margin

Rationale for Protocol Amendment

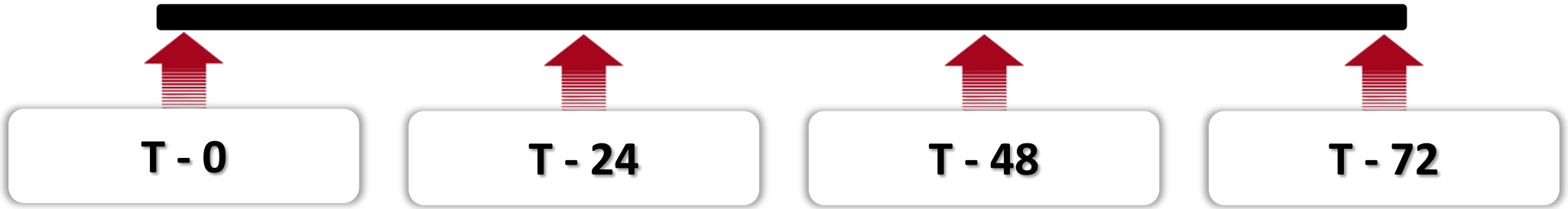
Rationale for Administrative Extension Cohort

INSPIRE Protocol Amendment

- Allow PGD component of the primary endpoint to comprehensively assess PGD3 within all time points rather than at single point post-transplantation (T72)

- Re-designate the Per-Protocol as primary analysis population for effectiveness

PGD3 Within 72 Hours Clinically Appropriate Endpoint for Preservation Technology



- PGD3 within 72 hours is comprehensive and robust assessment of PGD3 post-lung transplantation[1-4]
- Captures early timepoints that may be impacted by preservation injury as compared at only at T72
- PGD assessed at every timepoint throughout INSPIRE Trial

1. Whitson BA et al., JHLT 2007; 26:1004-1011
2. Daud et al., AMJ. Resp. & Crit. Care Med. 2007
3. Christie J et al., JHLT 2010; 29:2131-2137
4. Huang H et al., AJT 2008: 245402462

Per Protocol Analysis is Clinically Appropriate Population

- TransMedics consistently maintained that PP was appropriate primary analysis population:
  - FDA guidance on non-inferiority trial analysis[1]
  - PP assesses treatment effect when OCS and cold storage used as intended, eliminating confounding variables:
    - Not treated as randomized (e.g. OCS recipient transplanted using cold storage preserved lungs)
    - Major protocol violations (e.g. donor lung with pneumonia)

[1] US FDA - E9 Statistical Principals for Clinical Trials

Protocol Design Topics for Clarification

Protocol Non-Inferiority Design and Margin

Rationale for Protocol Amendment

Rationale for Administrative Extension Cohort

INSPIRE Trial Cohorts

- IDE approved 2 perfusion solutions in the OCS arm: OCS Lung Solution and LPD Solution
- Several investigators observed lung edema during preservation using LPD. TMDX notified FDA of this observation to seek advice
- Agreement to file an administrative extension (Admin Ext) to allow time to define plan
- OCS Solution subgroup identified as an important adjunct analysis

Comprehensive Data Presentation

- **Cohorts**
  - **INSPIRE Cohort** (N=320, pre-specified sample size)
  - **Combined Cohort** (N=349, INSPIRE + administrative extension)
- **Effectiveness Analysis Populations**
  - Per-protocol (primary)
  - Modified ITT (supportive)
- **Results presented both Overall and for OCS Solution Subgroup**

INSPIRE Trial Design

Abbas Ardehali, MD

Professor of Surgery and Medicine

William E. Connor Chair in Cardiothoracic Transplantation

Director, Heart and Lung Transplant Center

UCLA Medical Center

Donor Eligibility Criteria Reflect Standard Lung Transplantation

Inclusion	Exclusion
▪ Age <65 years old ▪ Normal gas exchange [PaO_2 / FiO_2 ≥ 300] at time of final acceptance of donor lung ▪ No active lung disease ▪ Lung suitable for both OCS or cold storage	▪ Presence of moderate to severe traumatic lung injury ▪ Presence of confirmed active pneumonia ▪ Positive serology (Hep. B/C, HIV etc.)

Recipient Eligibility Criteria Reflect Standard Lung Transplantation

Inclusion	Exclusion
▪ Registered double-lung transplant candidate ▪ Age ≥ 18 years old	▪ Prior solid organ or bone marrow transplant ▪ Multi-organ transplant recipient ▪ Single lung recipient ▪ Chronic renal failure

Primary Effectiveness Endpoint and Safety Endpoint

- Primary effectiveness composite endpoint (NI margin = 4%)
  - All-cause survival post transplant at day 30 **and** absence of PGD Grade 3 within first 72 hours
- Safety endpoint: mean # of lung-graft-related SAEs through 30 days post transplant (NI margin = 0.07 events)
  - Moderate to severe acute rejection
  - Respiratory failure
  - Bronchial anastomotic complications
  - Lung related infections
- 30-day window relevant to assessing preservation-related issues as compared to later timepoints which could be impacted by other variables

FDA Discussion Question 8

Secondary and Other Clinical Endpoints

- Secondary endpoints:
  - PGD Grade 3 at 72 hours (NI margin = 5%)
  - PGD Grade 2 or 3 at 72 hours (NI margin = 7.5%)
  - Patient survival at day 30 (NI margin = 4%)
- Other endpoints:
  - Bronchiolitis Obliterans Syndrome (BOS)
  - ICU length of stay
  - Hospital length of stay
  - Ventilation time

PGD Assessment According to ISHLT 2005 Consensus Statement[1]

Grade	PaO_2/FiO_2	Radiographic infiltrates consistent with pulmonary edema
0	>300	Absent
1	>300	Present
2	200-300	Present
3	<200	Present

- **Clinical Implementation of ISHLT Consensus Statement as follows:**
  - Intubated patients graded based on PaO_2/FiO_2 ratio & chest x-ray
  - Extubated patients graded 0/1 based chest x-ray
  - ECMO graded Grade 3 except prophylactic ECMO for IPAH

1. Christie et al. JHLT Oct 2005

FDA Discussion Question 4

PGD Grading Discrepancy Examples

Recipient **intubated**, PF ratio <200 mmHg with clear chest X-ray reading :

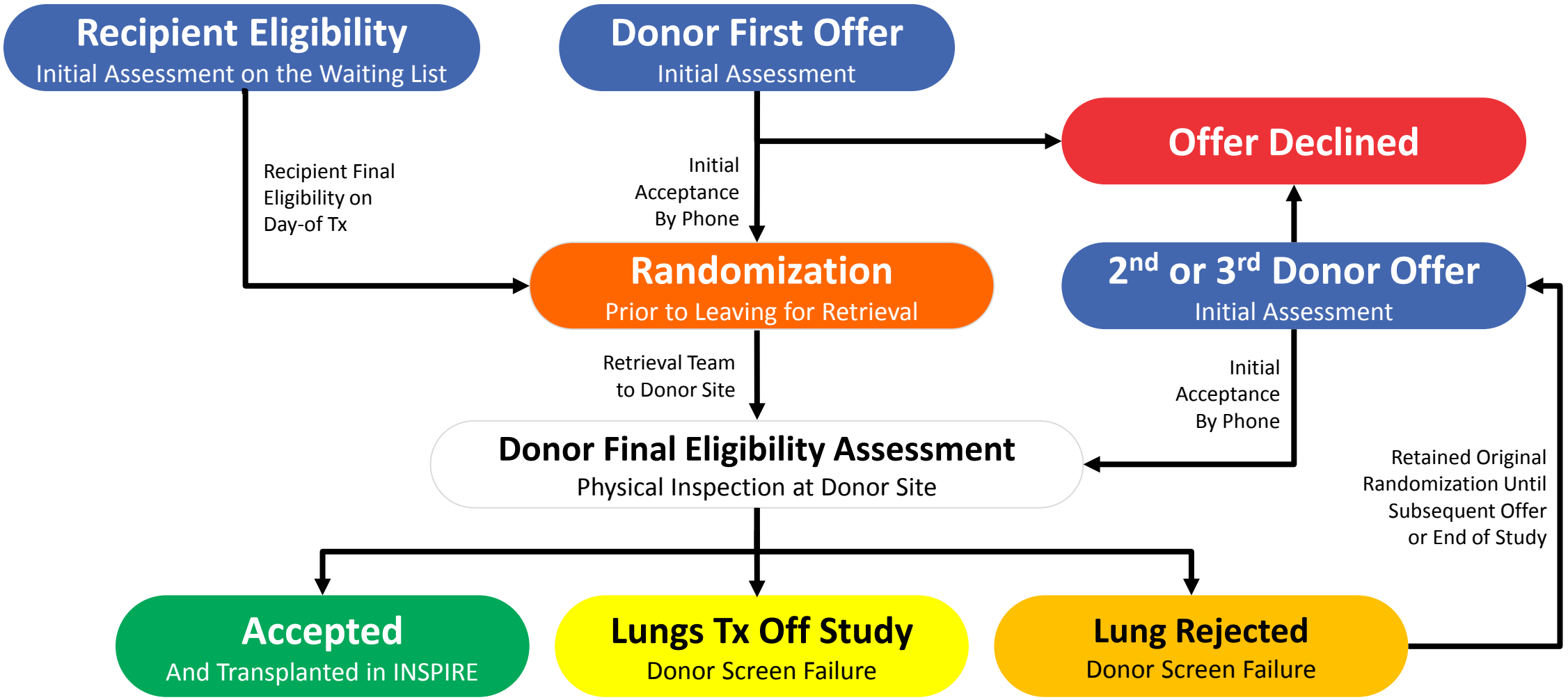
- INSPIRE Grade = PGD 3
- FDA Grade = PGD 0

Recipient **extubated**, PF ratio <200 mmHg on nasal supplemental O_2:

- INSPIRE Grade= PGD 0 or 1 based on Chest X-ray reading
- FDA Grade = PGD 3

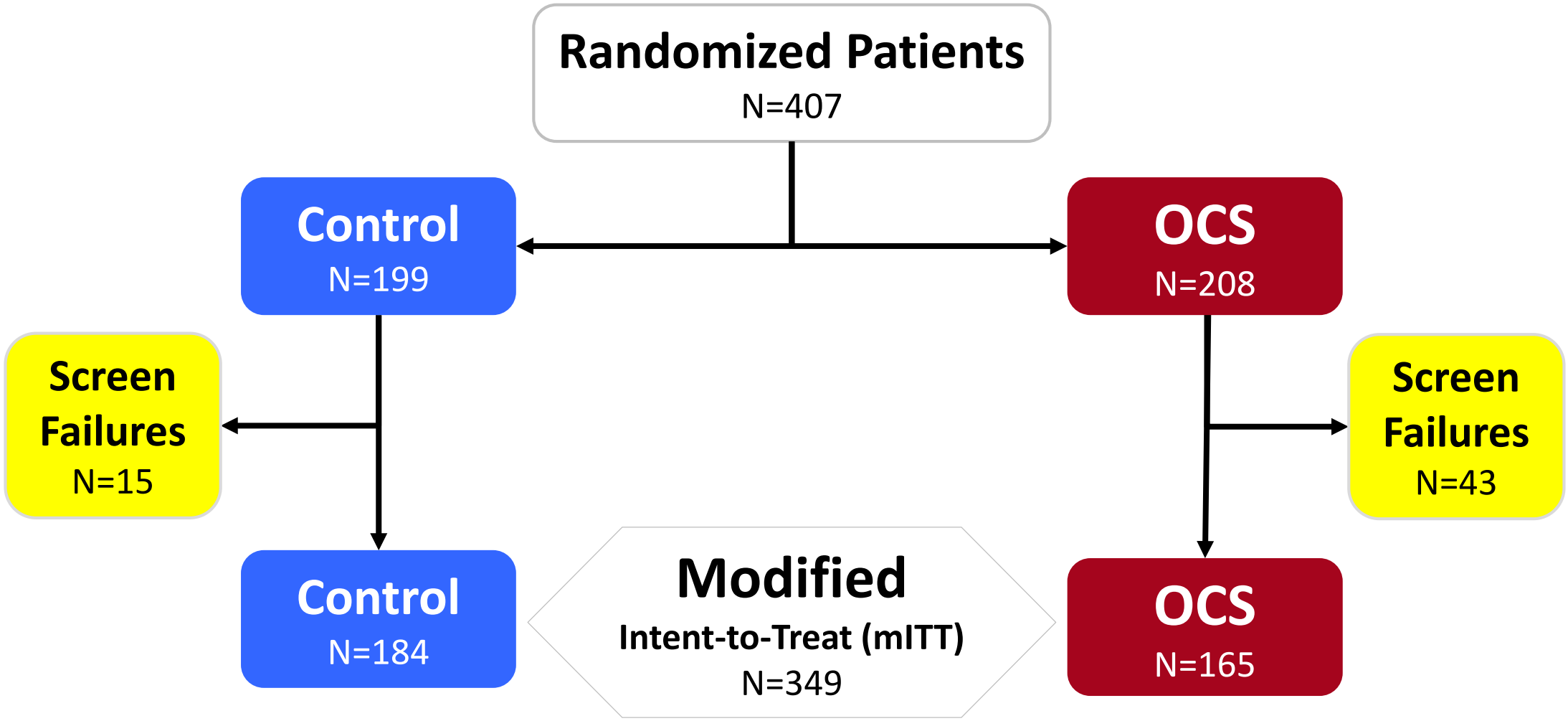
FDA Discussion Question 4

Complexities of Donor Lung Offer and Randomization Process



FDA Discussion Question 2

CONSORT Diagram of INSPIRE Trial (Randomization to mITT)



Categories of Screen Failures (n=58)

Screen Failure Type*	Definition	Control N=15	OCS N=43
Donor Screen Failure, Transplanted Off Study	Donor lungs **did not meet INSPIRE inclusion criteria** and were transplanted off study	**6**	**17**
Donor Screen Failure, Remained on Waiting List at End of Study	Initial donor lungs were **not accepted for transplantation**, patient remained randomized and waiting for a second offer at time of trial completion	**4**	**14**
Logistics	Logistical issues prevented use of randomized preservation method to be used	**1**	**10**
Recipient	Recipient found to be no longer eligible for inclusion in the trial on day of transplant	**4**	**2**

*Adjudicated by independent medical monitor

Extensive Analyses Performed To Understand Screen Failures

- **Multiple factors led to screen failures:**
  - Randomization prior to physical evaluation of donor lungs
  - Some lungs were not suitable for transplantation and randomized recipients remained on waiting list awaiting another donor offer
  - Transplant logistics
- No clear reason for imbalance between arms, however, this imbalance did not result in any measurable difference favoring the OCS arm in the patients analyzed in INSPIRE

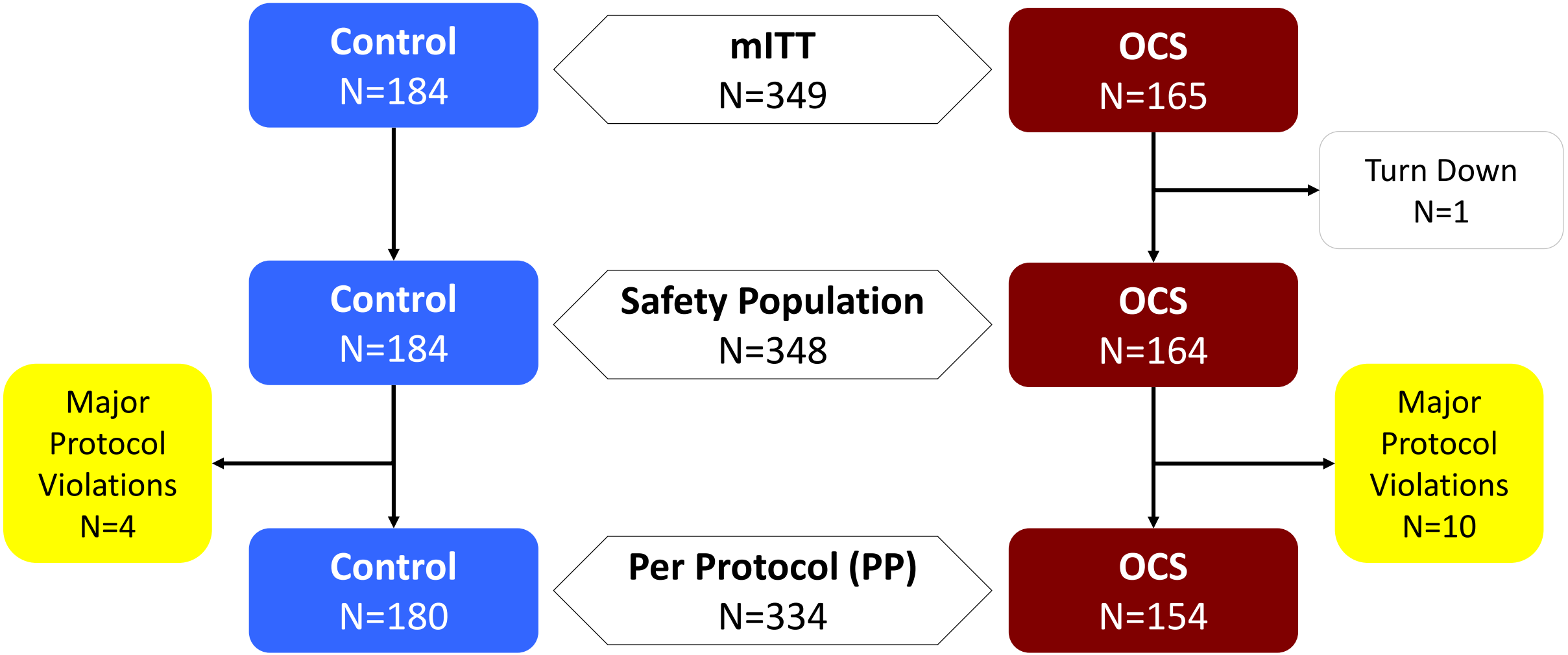
FDA Discussion Question #2

No Evidence of Donor Lung Characteristics Favoring OCS Arm in INSPIRE Trial

Donor Parameters	Control N=184	OCS N=165
Age (year) (mean ± SD)	**40 ± 14**	**42 ± 14**
Final PaO_2/FiO_2 (mean ± SD)	**432 ± 73**	**441 ± 79**
Smoking >20 Pky in last 6 months	**17%**	**18%**
Abnormal Findings on Donor Lung Visualization at Retrieval	**26%**	**36%**
Lung contusions	1%	4%
Emphysematous blebs	1%	2%
Granulomas	0.5%	2%
Pneumonia	0%	1%
Major atelectasis	21%	24%
Excessive lung adhesions, or parenchymal tears	**1%**	**6%**

FDA Discussion Question #2

CONSORT Diagram of INSPIRE Trial (mITT to PP)



Patients with Pre-Specified Major Protocol Violations Included in mITT, Not PP Population

Major Protocol Violation*	Control n=4	OCS n=10
Donor lungs not eligible for inclusion (active pneumonia, severe COPD with large blebs, or no final donor PF ratio to confirm eligibility)	1	4
Failure to follow Instruction for Use (IFU)/Protocol	3	4
Patient transplanted with preservation method different than randomized due to user error	0	2

*Adjudicated by independent medical monitor

Recipient Characteristics Similar Between Arms

Recipient Characteristic	Control N=184	OCS N=165
Age (years), Mean ± SD	50 ± 14	50 ± 13
Female, %	36%	48%
BMI (kg/m^2), Mean ± SD	23 ± 4.1	23 ± 4.6
LAS Score, Mean ± SD	48 ± 18	51 ± 20
On ECMO on Transplant Day, %	5%	5%
Use of Intraoperative Cardiopulmonary Bypass	38%	40%
Secondary Pulmonary Hypertension, %	32%	40%
Primary Cause of Lung Failure, %		
COPD	28%	28%
IPF	34%	35%
Cystic Fibrosis	23%	21%
IPAH	4%	9%
Sarcoidosis	5%	3%

INSPIRE Trial Methodology Summary

- INSPIRE RCT was successfully implemented in 21 international academic lung Tx. Centers in the complex field of lung transplantation
- PGD assessment followed the clinical implementation of the 2005 ISHLT Consensus Statement
- Screen failure imbalance did not result in any measurable difference favoring the OCS arm
- Largest body of prospective clinical evidence supporting use of EVLP in standard lung transplantation

INSPIRE Trial Adjudication and Trial Oversight

John Wallwork, FRCS, FmedSCI
Emeritus Professor, Cardiothoracic Surgery
Papworth Hospital
Cambridge University, UK

President (1994-95), International Society for Heart and Lung Transplant (ISHLT)

Medical Monitor Adjudication Process

- Adjudicated PGD scores according to the ISHLT 2005 consensus statement guidelines. This process was implemented in a blinded and consistent manner for both study groups.

- Adjudicated all Serious Adverse Events (SAEs) according to the protocol definitions, without changes to the protocol safety endpoint definition. This process was implemented in a blinded and consistent manner for both study groups

- There was no conflict between Medical Monitor role and my role on the DSMB

FDA Discussion Question 5

INSPIRE Trial Results

Gregor Warnecke, MD, PhD

Vice Chairman

Director of Heart and Lung Transplantation

Hannover Medical School

Outline of INSPIRE Trial Results

Critical Transplant Times and OCS Perfusion Parameters

Composite Primary Effectiveness Endpoint

Components of Primary Composite Endpoint

Short-Term Patient Survival

Freedom from PGD3 Within 72 hours

Adjunct Effectiveness Analysis

Secondary Endpoints

Safety

Additional Clinical Endpoints

INSPIRE Trial Definitions of Cross-Clamp and Ischemic Times

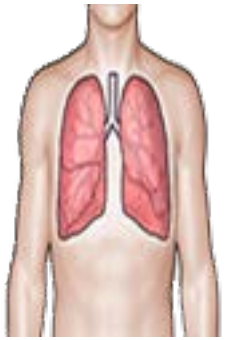
	Definition
Cross-Clamp Time	Time from aortic cross-clamp in donor to pulmonary artery cross-clamp removal in recipient
Ischemic Time	Time donor lung was not perfused with oxygenated blood

OCS Lung Perfusion Impact on Ischemic Times During Transplantation

Control - Cross Clamp/Ischemic Times Are Same

Donor

- From aortic cross-clamp in donor to pulmonary artery cross-clamp removal in recipient
- Time donor lung was not perfused with oxygenated blood

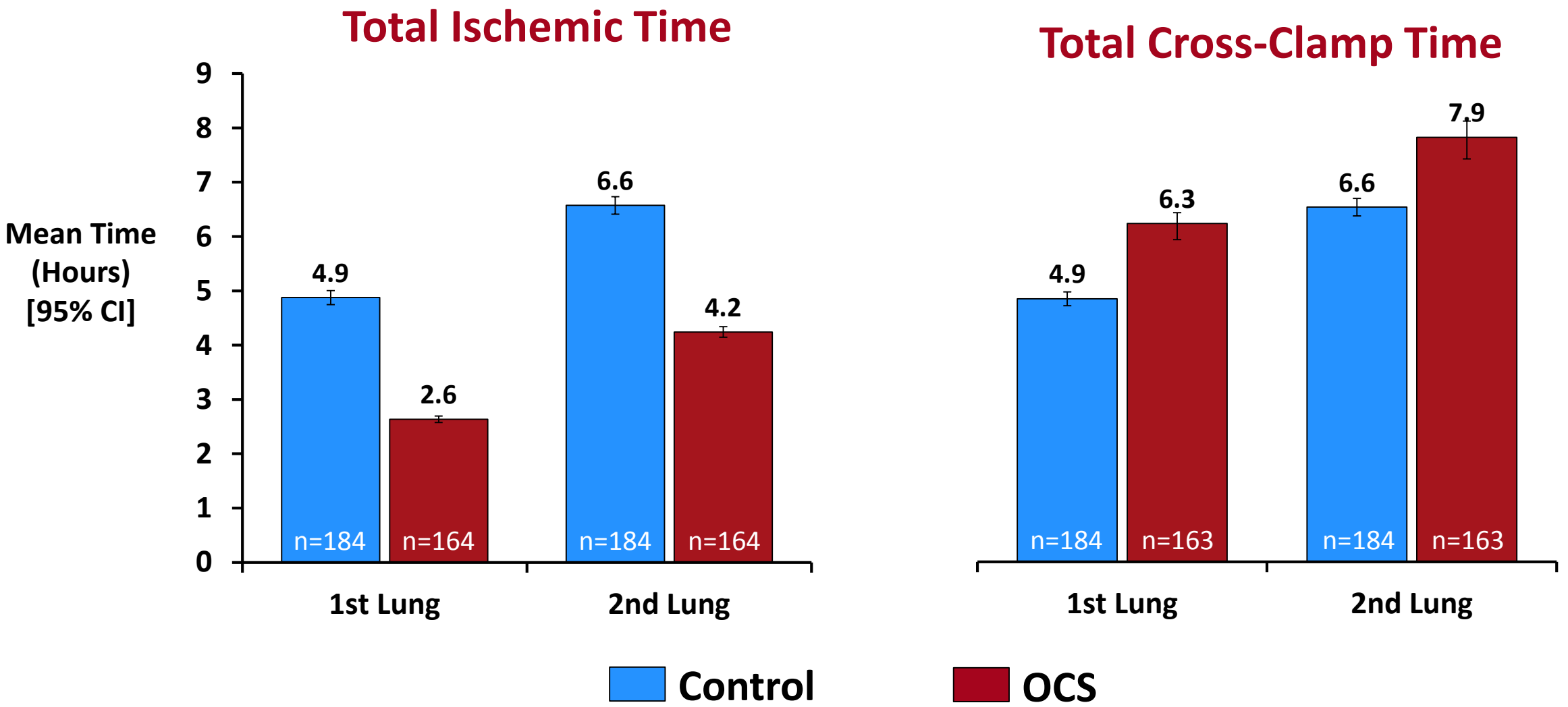


Recipient

OCS - Ischemic Times Are Limited Due to OCS Perfusion

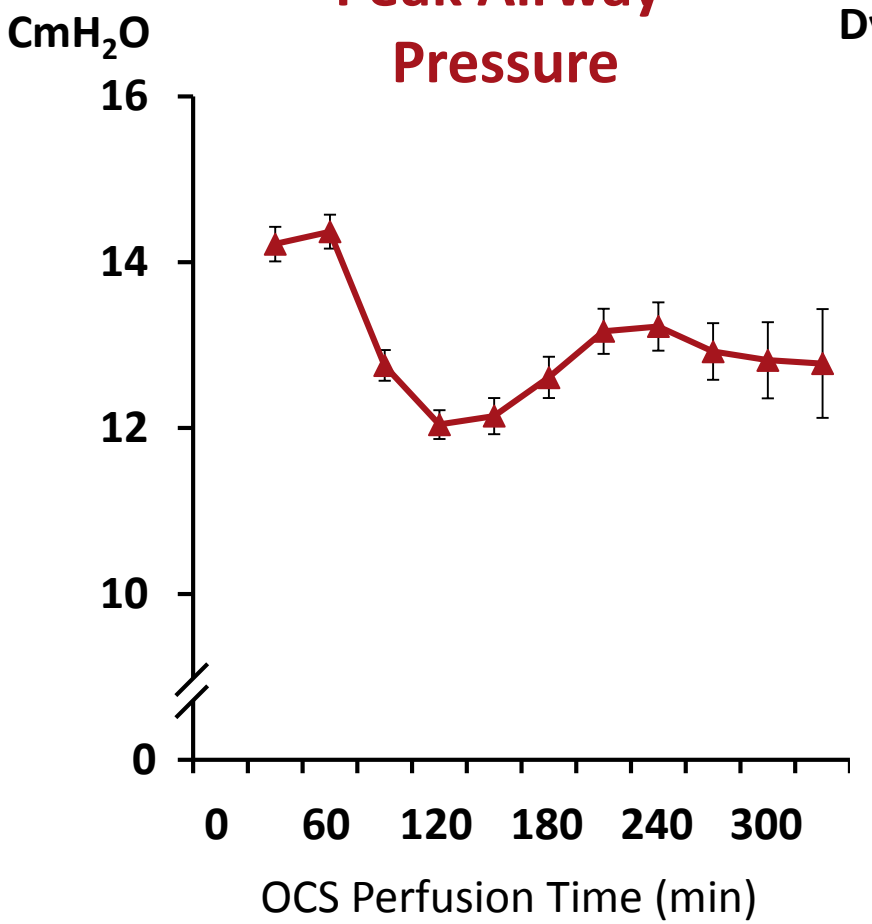
Ischemia | Oxygenated Perfusion | Ischemia

OCS Significantly Reduced Ischemic Time on Donor Lungs – Combined Cohort

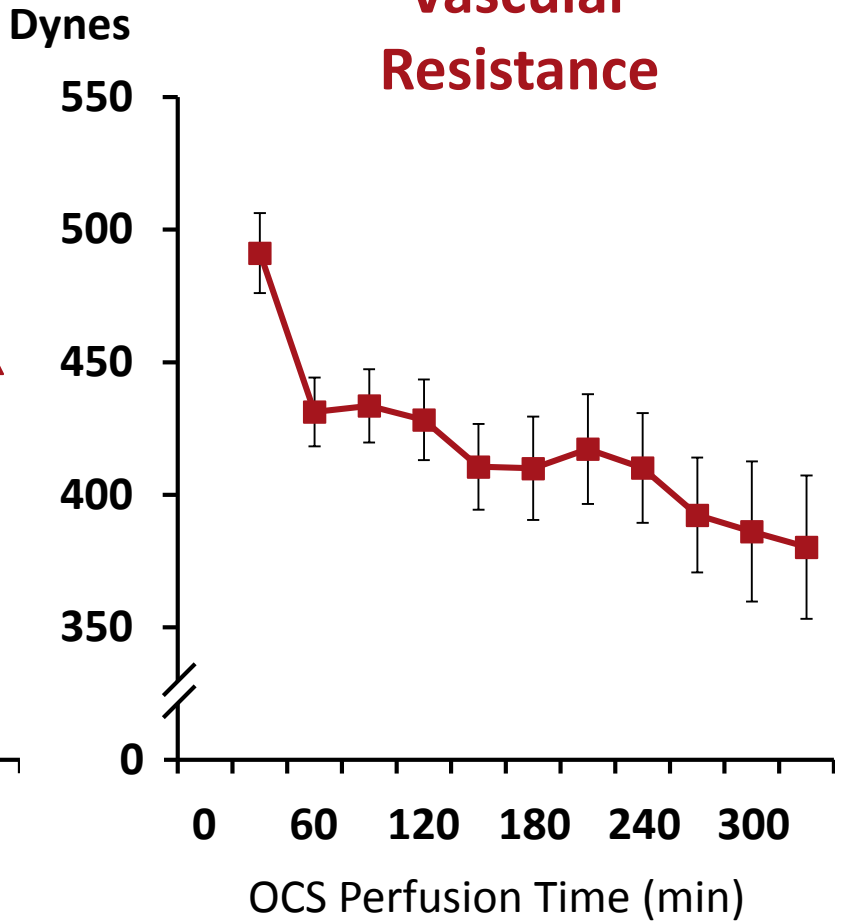


Stable Perfusion Parameters & Lung Oxygenation on OCS Lung System – Combined Cohort

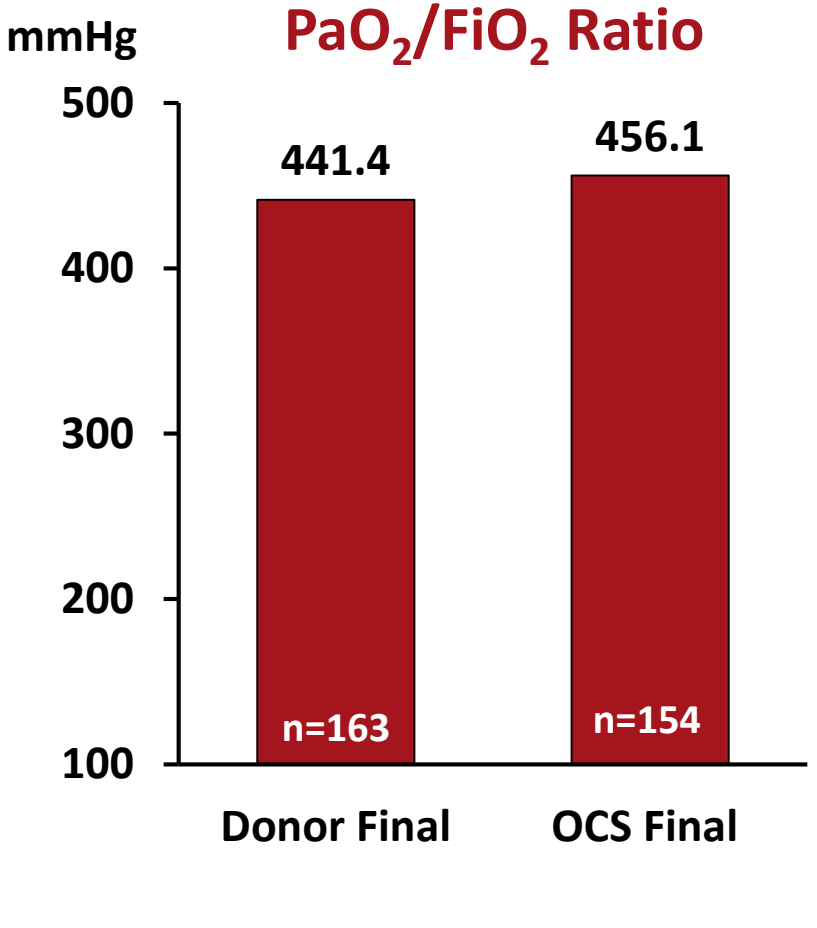
Peak Airway Pressure



Vascular Resistance



PaO_2/FiO_2 Ratio



Mean± SE

Outline of INSPIRE Trial Results

Critical Transplant Times and OCS Perfusion Parameters

Composite Primary Effectiveness Endpoint

Components of Primary Composite Endpoint

Short-Term Patient Survival

Freedom from PGD3 Within 72 hours

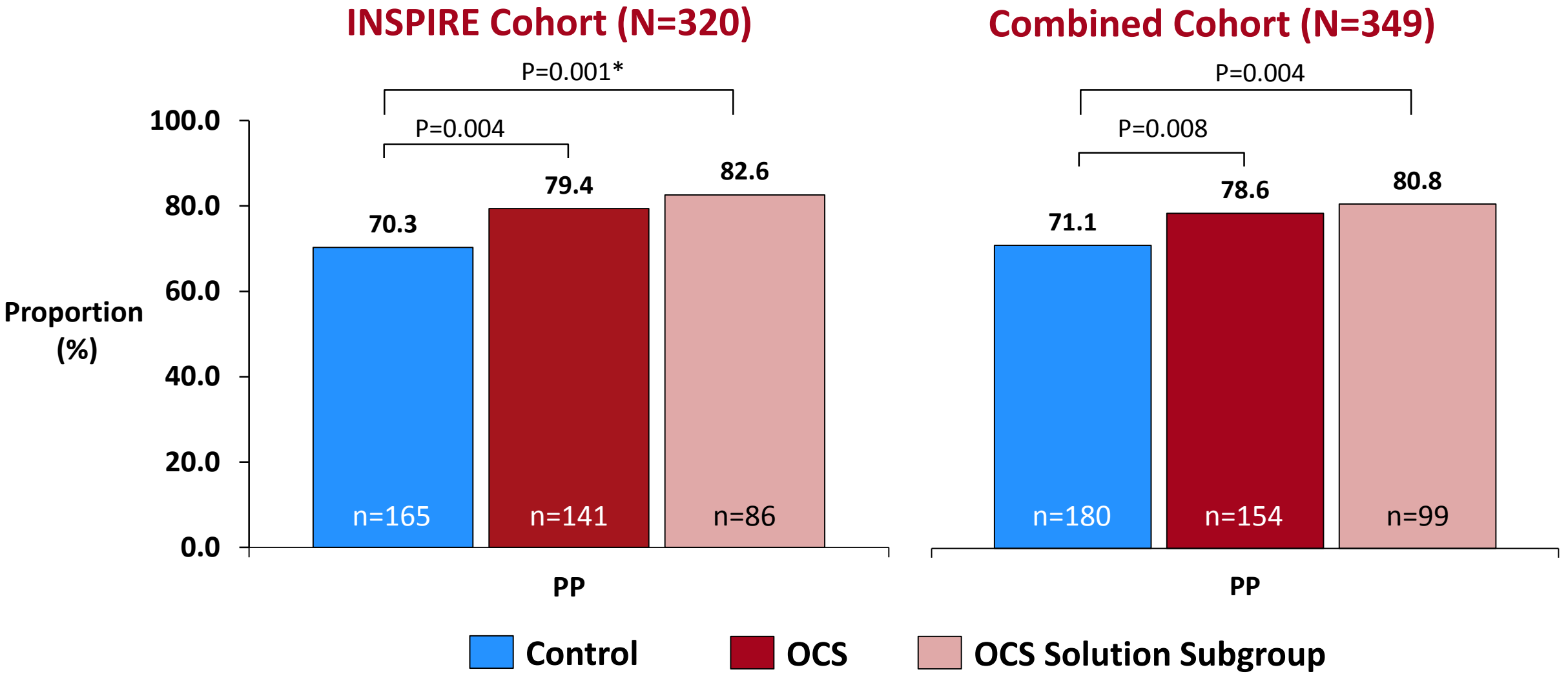
Adjunct Effectiveness Analysis

Secondary Endpoints

Safety

Additional Clinical Endpoints

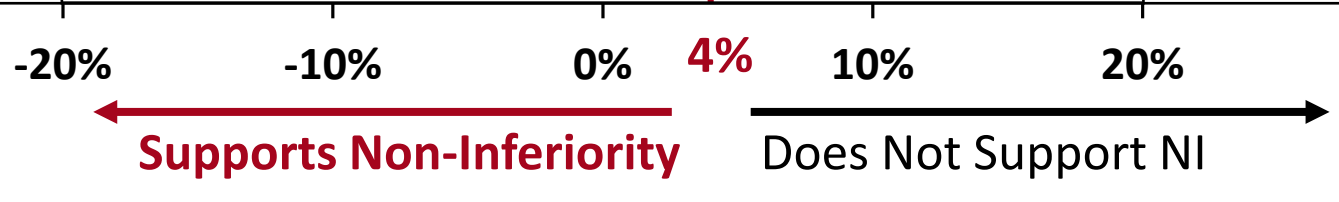
Primary Effectiveness Endpoint - PP:
Composite of 30-Day Survival and Freedom from PGD3 Within 72 Hours



* met superiority test

INSPIRE Trial Met Pre-specified Primary Effectiveness Endpoint

		Point Estimate		Treatment Difference [Upper 95% CI]	P-value
OCS Overall		**Control**	**OCS**		
PP	INSPIRE Cohort	70.3%	79.4%	-9.1%	0.004
	Combined Cohort	71.1%	78.6%	-7.5%	0.008
mITT	INSPIRE Cohort	70.4%	74.2%	-3.8%	0.060
	Combined Cohort	71.2%	73.3%	-2.1%	0.100
OCS Solution					
PP	INSPIRE Cohort	70.3%	82.6%	-12.3%	0.001
	Combined Cohort	71.1%	80.8%	-9.7%	0.004
mITT	INSPIRE Cohort	70.4%	78.9%	-8.5%	0.012
	Combined Cohort	71.2%	76.9%	-5.7%	0.034



Outline of INSPIRE Trial Results

Critical Transplant Times and OCS Perfusion Parameters

Composite Primary Effectiveness Endpoint

Components of Primary Composite Endpoint

Short-Term Patient Survival

Freedom from PGD3 Within 72 hours

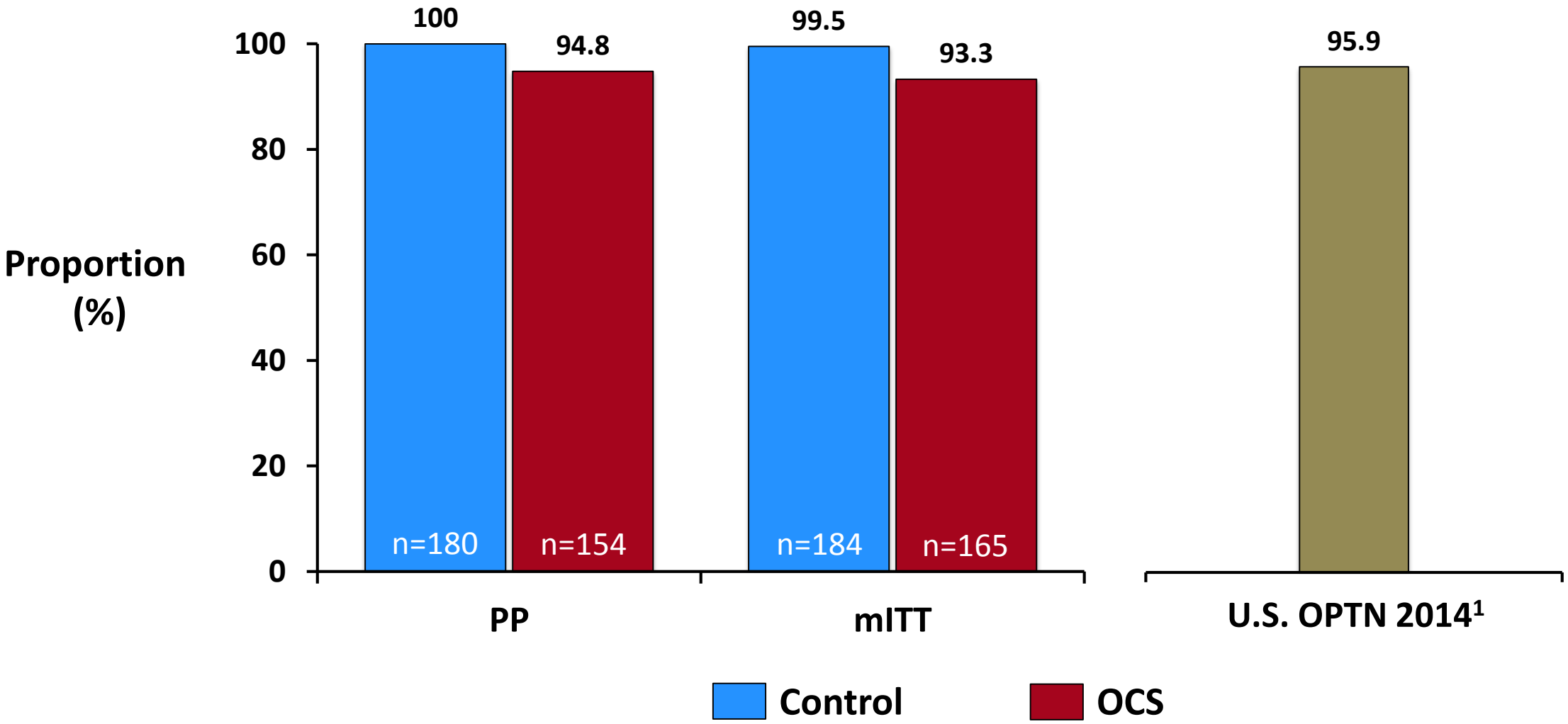
Adjunct Effectiveness Analysis

Secondary Endpoints

Safety

Additional Clinical Endpoints

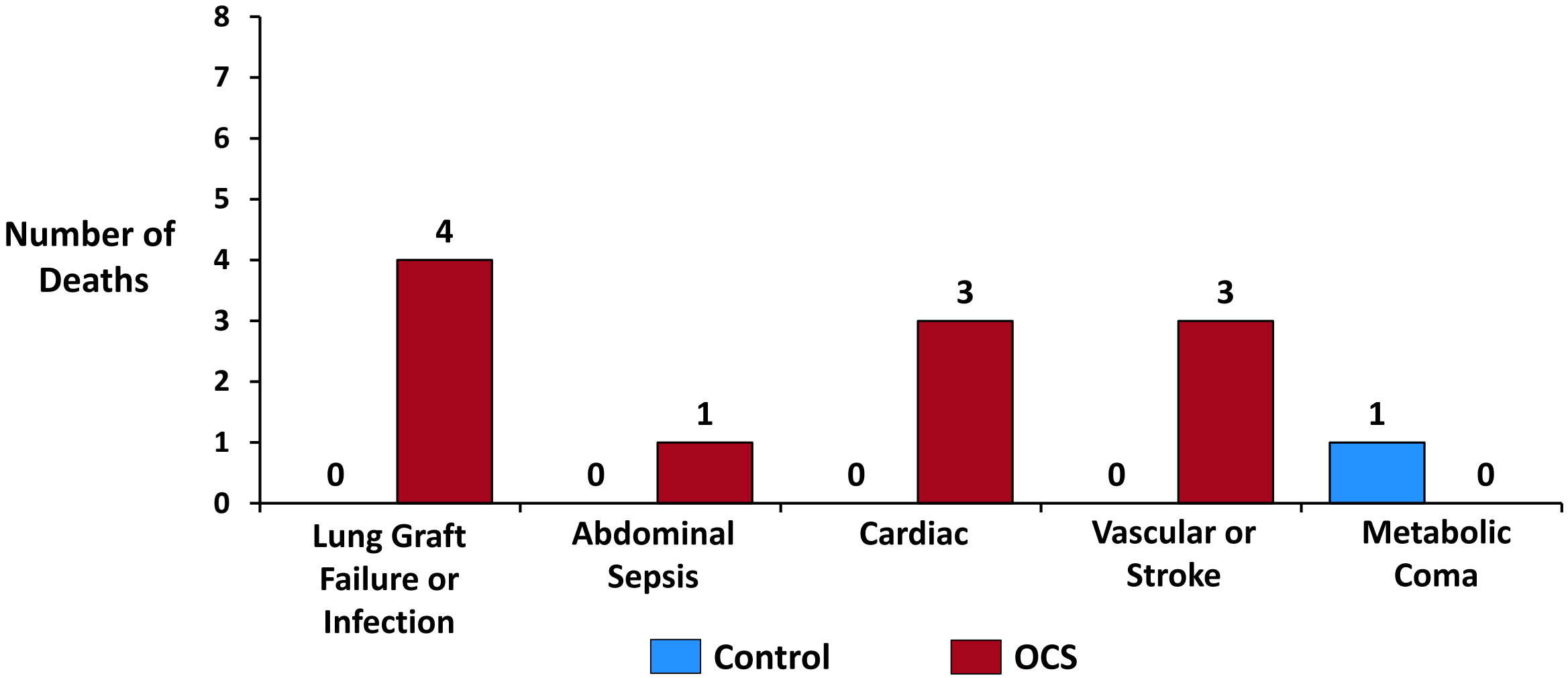
30-Day Patient Survival – Combined Cohort



1. 2014 U.S. OPTN/SRTR Annual Report

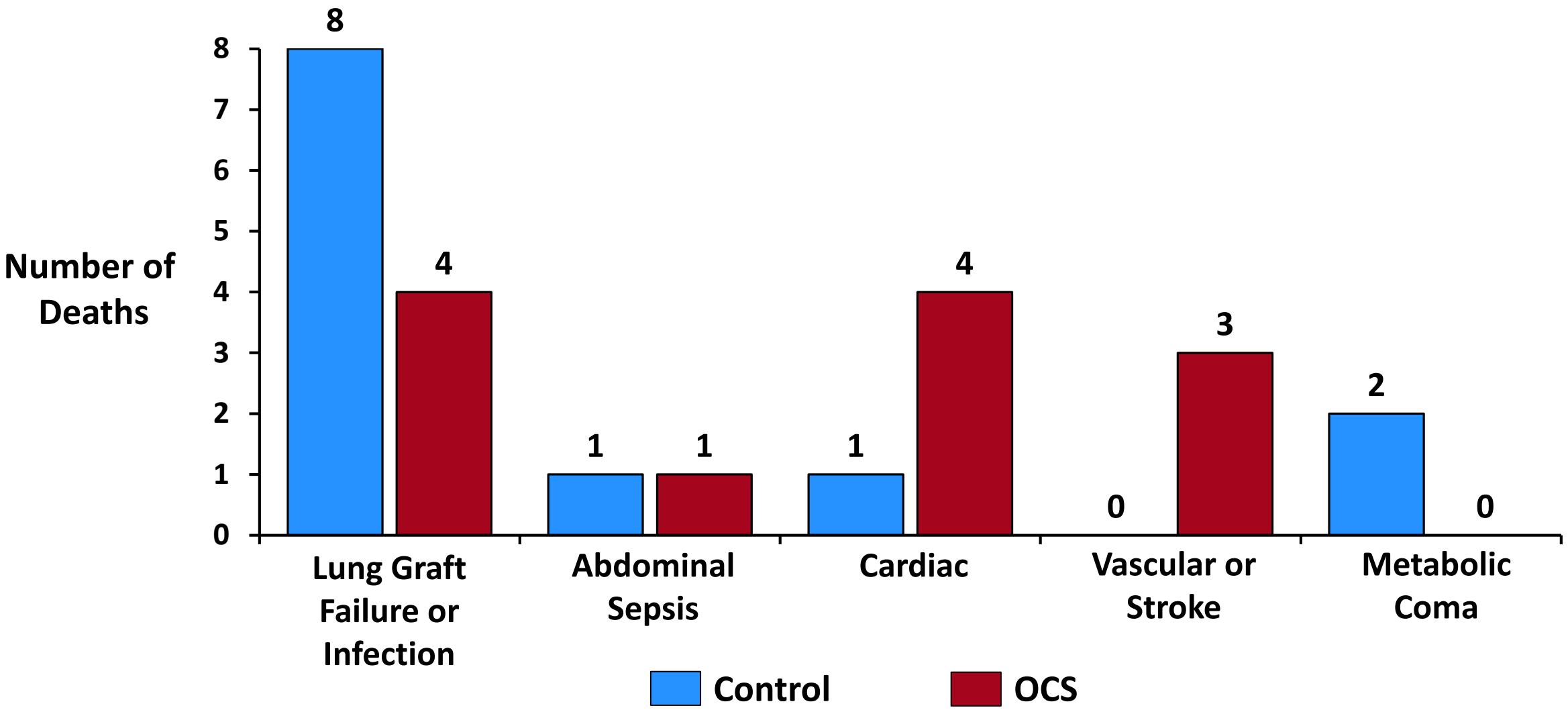
FDA Discussion Question 6

30-Day All Causes of Mortality – Combined Cohort



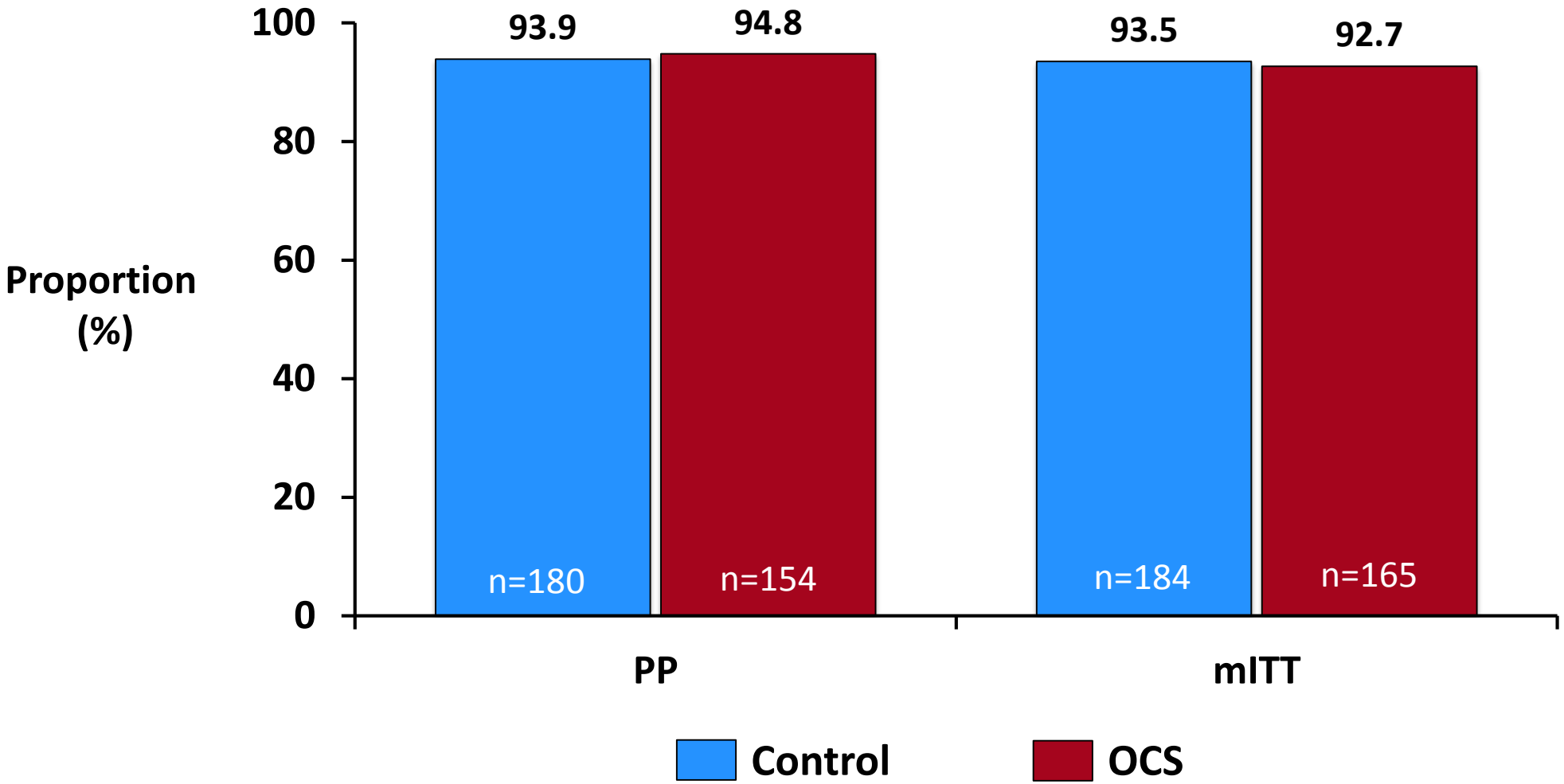
FDA Discussion Question 6

30-Day AND In-Hospital Causes of Mortality - Combined Cohort



FDA Discussion Question 6

30-Day AND In-Hospital Survival - Combined Cohort



FDA Discussion Question 6

Outline of INSPIRE Trial Results

Critical Transplant Times and OCS Perfusion Parameters

Composite Primary Effectiveness Endpoint

Components of Primary Composite Endpoint

Short-Term Patient Survival

Freedom from PGD3 Within 72 hours

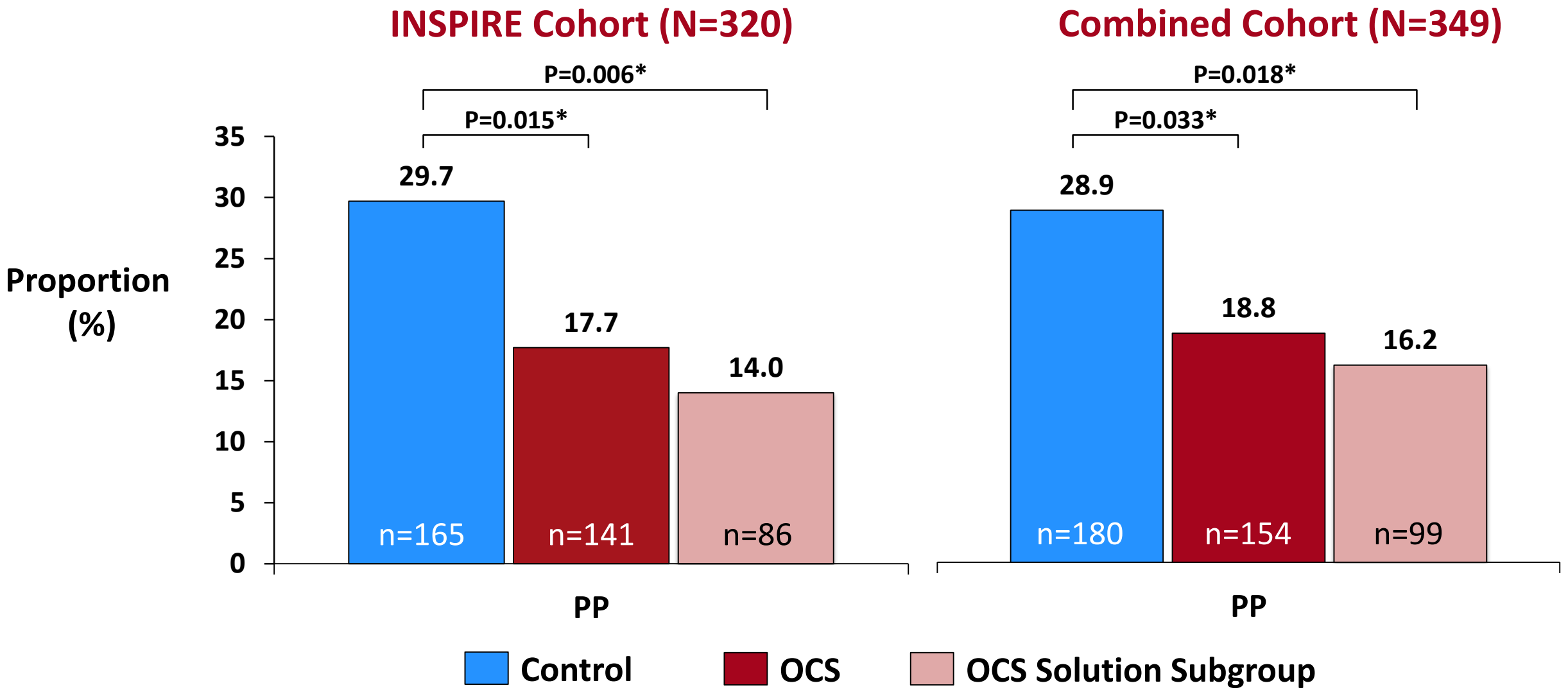
Adjunct Effectiveness Analysis

Secondary Endpoints

Safety

Additional Clinical Endpoints

OCS Resulted in Significant Reduction of PGD3 Within 72 Hours



* superiority test

Outline of INSPIRE Trial Results

Critical Transplant Times and OCS Perfusion Parameters

Composite Primary Effectiveness Endpoint

Components of Primary Composite Endpoint

Short-Term Patient Survival

Freedom from PGD3 Within 72 hours

Adjunct Effectiveness Analysis

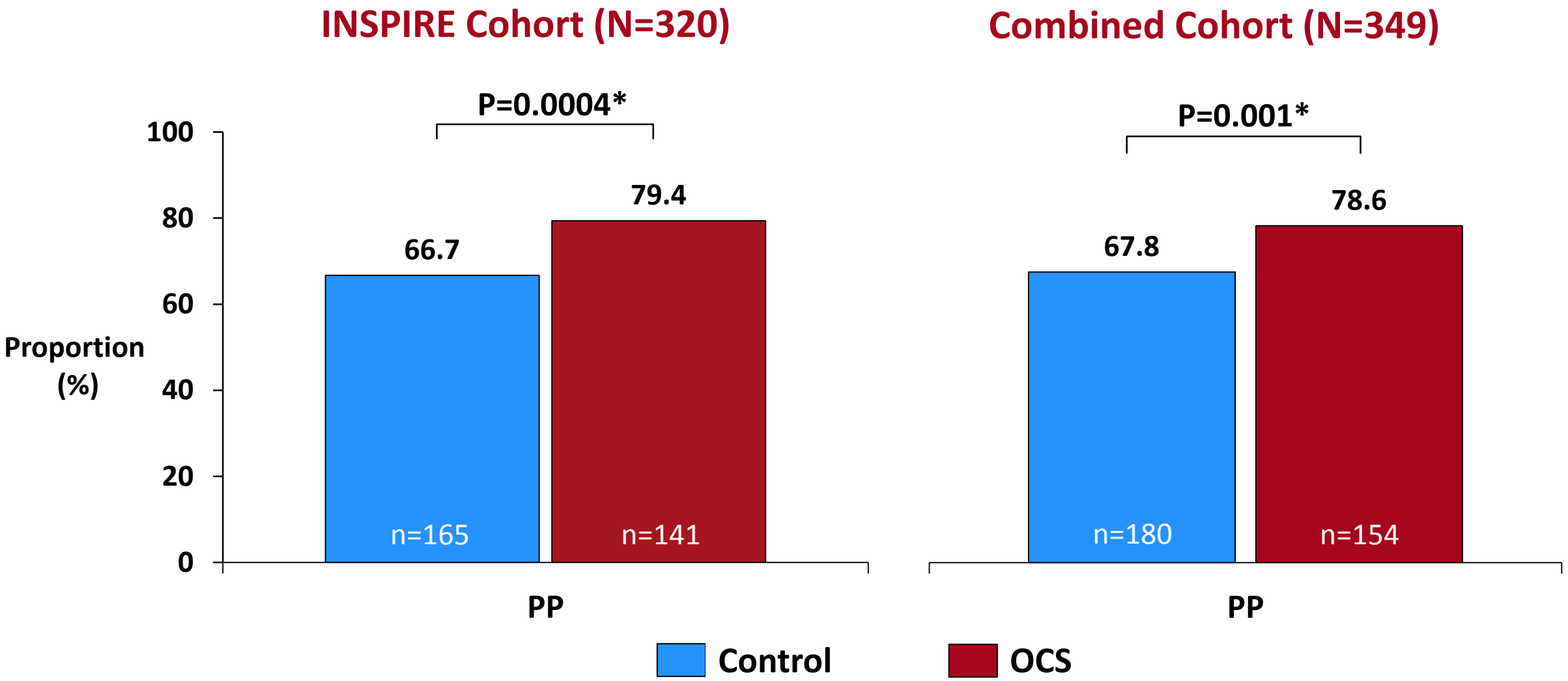
Secondary Endpoints

Safety

Additional Clinical Endpoints

Post-Hoc Adjunct Effectiveness Analysis – PP :

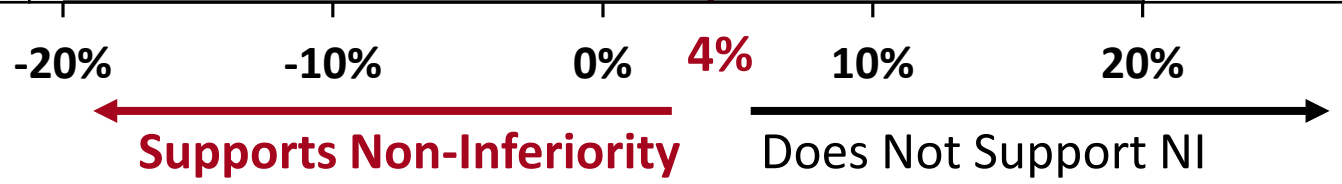
Composite of 30-Day and In-Hospital Survival & Freedom from PGD3 Within 72 Hours



* met superiority test

Post-Hoc Adjunct Effectiveness Analysis Demonstrates Consistent Benefit of OCS

		Point Estimate		Treatment Difference [Upper 95% CI]	P-value
OCS Overall		**Control**	**OCS**		
PP	INSPIRE Cohort	66.7%	79.4%	-12.8%	0.0004
	Combined Cohort	67.8%	78.6%	-10.8%	0.001
mITT	INSPIRE Cohort	66.9%	74.2%	-7.3%	0.013
	Combined Cohort	67.9%	73.3%	-5.4%	0.027
OCS Solution					
PP	INSPIRE Cohort	66.7%	82.6%	-15.9%	0.0001
	Combined Cohort	67.8%	80.8%	-13.0%	0.0006
mITT	INSPIRE Cohort	66.9%	78.9%	-12.0%	0.002
	Combined Cohort	67.9%	76.9%	-9.0%	0.008



Outline of INSPIRE Trial Results

Critical Transplant Times and OCS Perfusion Parameters

Composite Primary Effectiveness Endpoint

Components of Primary Composite Endpoint

Short-Term Patient Survival

Freedom from PGD3 Within 72 hours

Adjunct Effectiveness Analysis

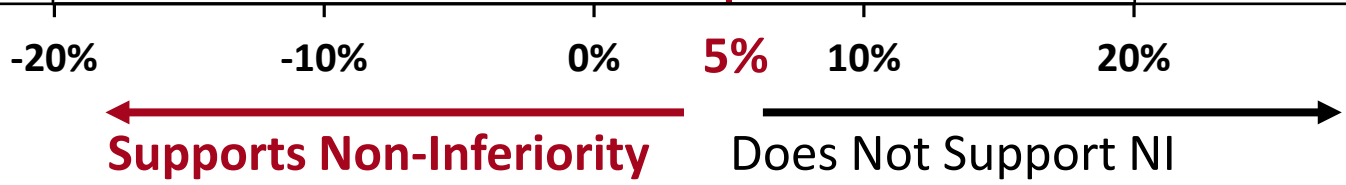
Secondary Endpoints

Safety

Additional Clinical Endpoints

Rate of PGD Grade 3 At 72 Hours Similar Between Arms

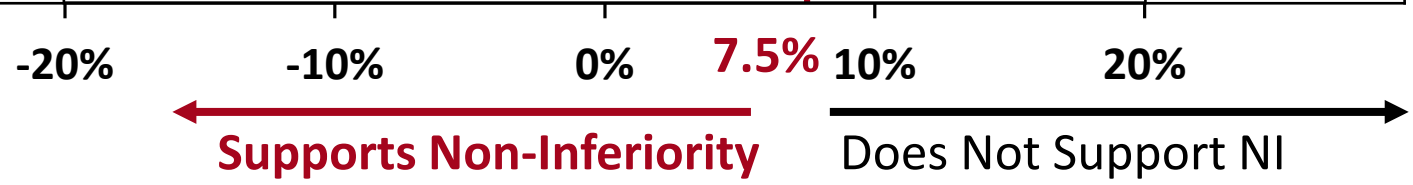
		Point Estimate		Treatment Difference [Upper 95% CI]	P-value
OCS Overall		**Control**	**OCS**		
PP	INSPIRE Cohort	4.2%	2.1%	-2.1%	0.0002
	Combined Cohort	5.0%	3.9%	-1.1%	0.003
mITT	INSPIRE Cohort	4.7%	5.3%	0.6%	0.037
	Combined Cohort	5.5%	6.7%	1.2%	0.072
OCS Solution					
PP	INSPIRE Cohort	4.2%	2.3%	-1.9%	0.001
	Combined Cohort	5.0%	5.1%	0.0%	0.035
mITT	INSPIRE Cohort	4.7%	4.5%	-0.2%	0.028
	Combined Cohort	5.5%	6.8%	1.3%	0.110



FDA Discussion Question 1

Rate of PGD Grade 2 or 3 At 72 Hours Similar Between Arms

		Point Estimate		Treatment Difference [Upper 95% CI]	P-value
OCS Overall		**Control**	**OCS**		
PP	INSPIRE Cohort	8.5%	11.3%	2.9%	0.089
	Combined Cohort	10.6%	13.0%	2.4%	0.075
mITT	INSPIRE Cohort	8.9%	15.3%	6.5%	0.388
	Combined Cohort	10.9%	16.5%	5.5%	-
OCS Solution					
PP	INSPIRE Cohort	8.5%	7.0%	-1.5%	0.005
	Combined Cohort	10.6%	10.1%	-0.5%	0.018
mITT	INSPIRE Cohort	8.9%	9.0%	0.1%	0.024
	Combined Cohort	10.9%	11.7%	0.7%	-



Outline of INSPIRE Trial Results

Critical Transplant Times and OCS Perfusion Parameters

Composite Primary Effectiveness Endpoint

Components of Primary Composite Endpoint

Short-Term Patient Survival

Freedom from PGD3 Within 72 hours

Adjunct Effectiveness Analysis

Secondary Endpoints

Safety

Additional Clinical Endpoints

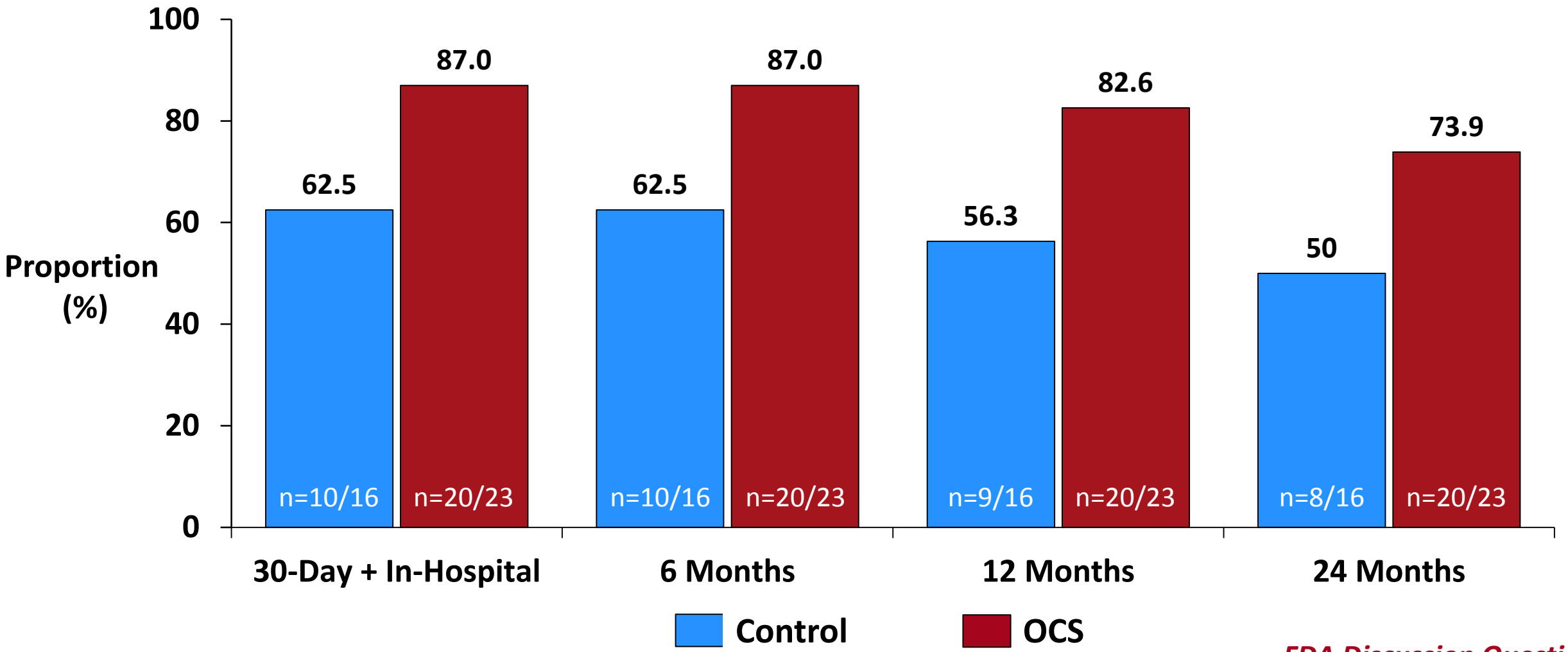
OCS Lung System Met Primary Safety Endpoint

INSPIRE Combined Cohort (n=349)	Control N=184	OCS N=164
Lung-graft related SAEs, n (%)	45 (24.5)	40 (24.4)
Mean ± SD	0.29 ± 0.54	0.26 ± 0.48
Non-Inferiority p-value		0.042
Type of Lung-graft related SAEs, n (%)		
Acute Rejection	4 (2)	2 (1)
Respiratory Failure*	16 (9)	23 (14)
Bronchial Anastomotic Complication	4 (2)	0
Major Pulmonary-Related Infection	29 (16)	18 (11)

* Need for re-intubation, tracheostomy or the inability to discontinue ventilator support within 4 days post-transplant

FDA Discussion Question 8

Survival Profile for Respiratory Failure Patients



FDA Discussion Question 8

Overall Safety Profile (including Mortality) Similar Between OCS and Control

Patients	Control N=184	OCS N=164
Any Type of AE	83%	83%
Definitely Related	0%	0%
Probably Related	0%	1%
Possibly Related	3%	3%
Unlikely Related	31%	36%
Not Related	71%	69%
Any SAEs	63%	56%
Any Severe AEs	29%	31%
Death up to 24 months	16%	16%

Outline of INSPIRE Trial Results

Critical Transplant Times and OCS Perfusion Parameters

Composite Primary Effectiveness Endpoint

Components of Primary Composite Endpoint

Short-Term Patient Survival

Freedom from PGD3 Within 72 hours

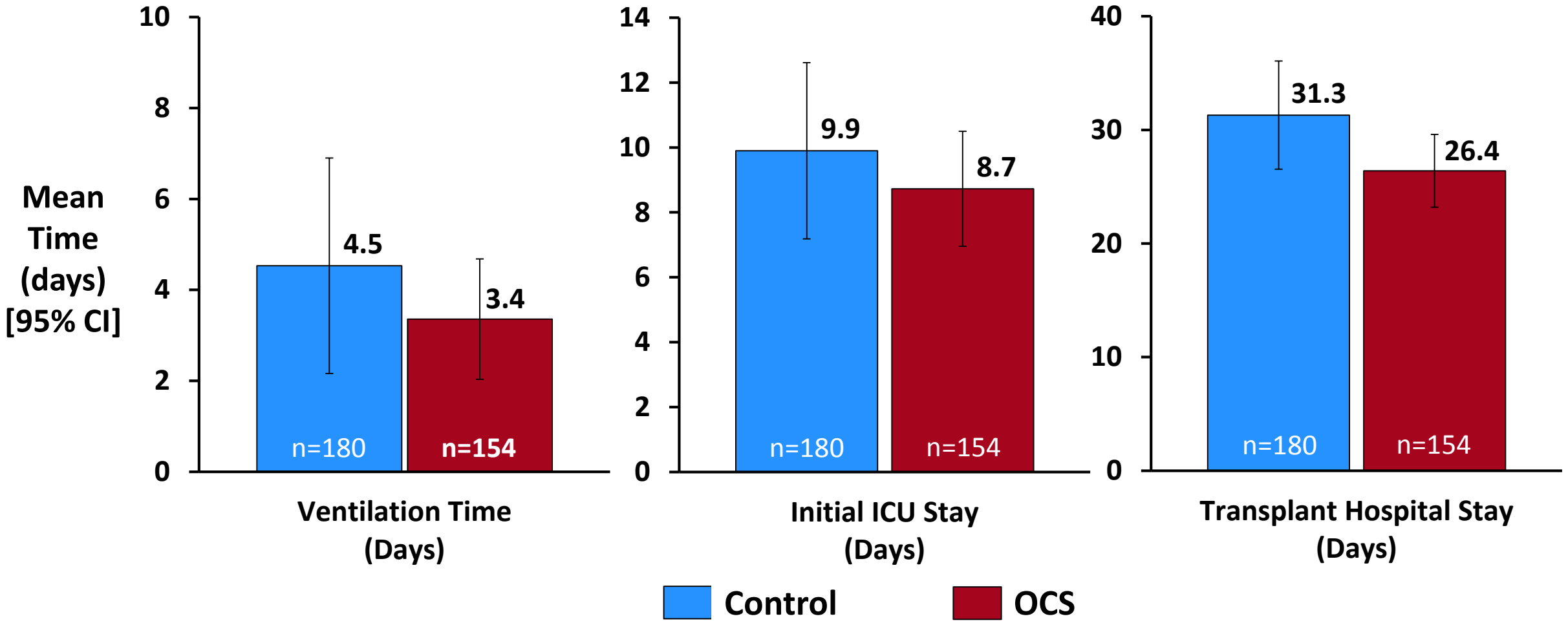
Adjunct Effectiveness Analysis

Secondary Endpoints

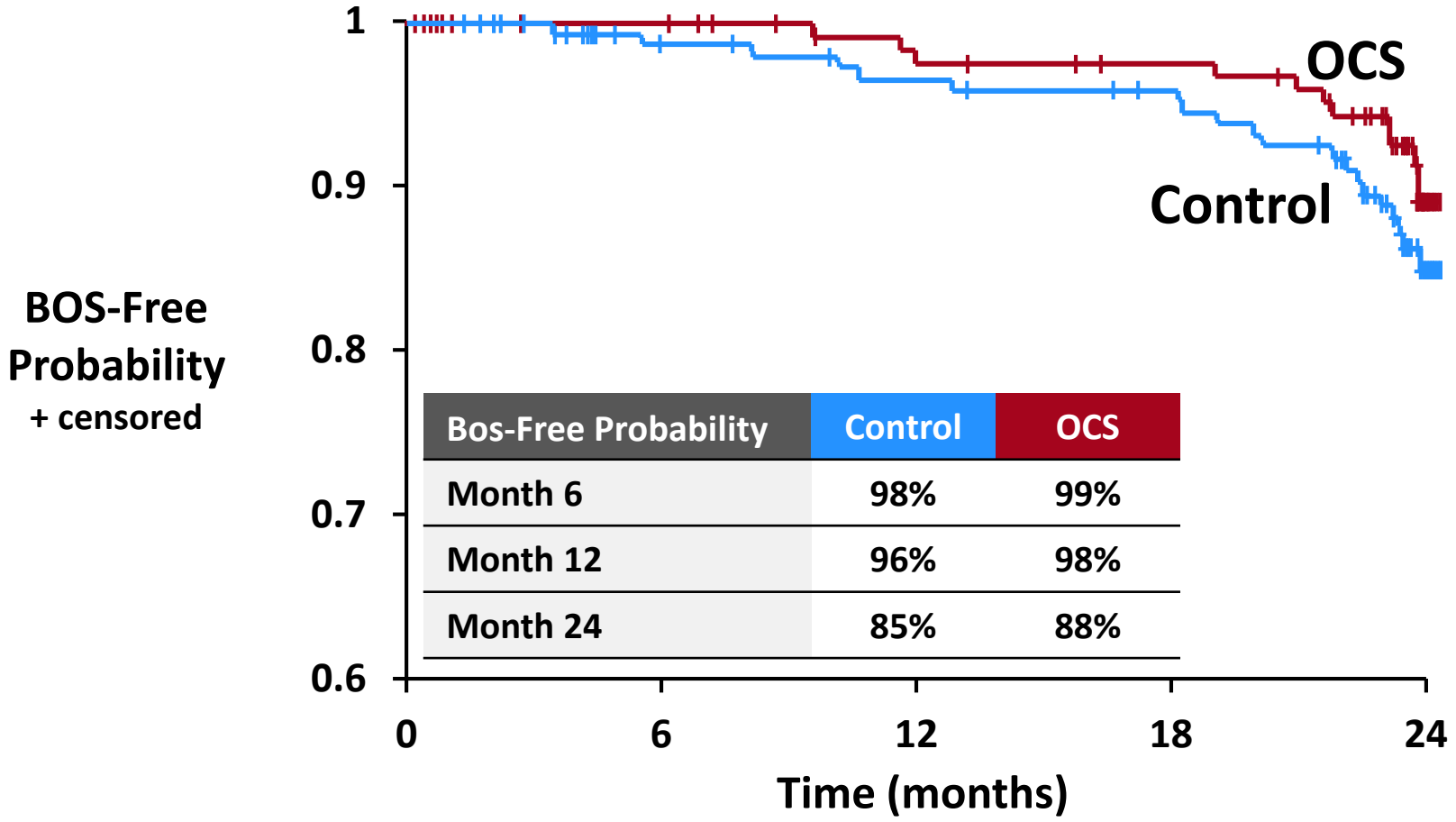
Safety

Additional Clinical Endpoints

Ventilation Times, Lengths of ICU and Initial Hospital Stay Comparisons – Combined Cohort



OCS Associated with Lower Incidence of BOS Through 24 Months – Combined Cohort PP



Bos-Free Probability	Control	OCS
Month 6	98%	99%
Month 12	96%	98%
Month 24	85%	88%

# at risk					
OCS	154	143	134	130	76
Control	180	162	153	143	56

FDA Discussion Question 9

INSPIRE Trial Demonstrated Safety and Effectiveness of the OCS Lung System

- Met primary effectiveness endpoint and safety endpoint
- Significant reduction of PGD3 within 72 hours
- Significant reduction of ischemic time on donor lungs
- No additional safety risk associated with OCS compared to Control
- Favorable 2-year BOS results to be further evaluated in post-approval study

Training Program and Post-Market Study Plan

Waleed Hassanein, MD

President and CEO

TransMedics, Inc.

Clinical Training Infrastructure

- Dedicated 15,000 Sq. F. facility equipped with latest surgical and diagnostics equipment to replicate a retrieval environment
- 86 global academic and clinical institutions
- >400 health care professionals trained


TransMedics


TransMedics
TransMedics
TransMedics

OCS Clinical Training and Support Program

- Initial Hands-On Clinical Training and Certification of Every New Clinical Center Starting an OCS Lung Program
- Dedicated OCS Lung iPad Training & Support Application
- 24 X 7 Phone and Text Messaging Hotline

Post Approval Study Plan

Two-Part Post-Approval Study Plan

- **Long-term Follow-up of INSPIRE Patients**
- **OCS Thoracic Organ Perfusion (TOP) Registry**

FDA Discussion Question 12 & 13

Long-Term Follow-up of INSPIRE Patients

Goal

- Assess impact of OCS Lung preservation on the incidence of BOS and survival for up to 5 years

Data Collection

- Incidence of BOS at year 3, 4, and 5
- Survival at year 3, 4, and 5

FDA Discussion Question 12 & 13

OCS Thoracic Organ Perfusion Registry

- **Goal:** Expand clinical evidence for OCS Lung System in standard criteria lung transplantation post market
- **Primary Clinical Objective**: 5-year survival compared to SRTR/OPTN data for historical controls in same time period of enrollment
- **Other Clinical Objectives:**
  - Incidence of PGD within initial 72 hours
  - Incidence of BOS-free survival up to 5 years

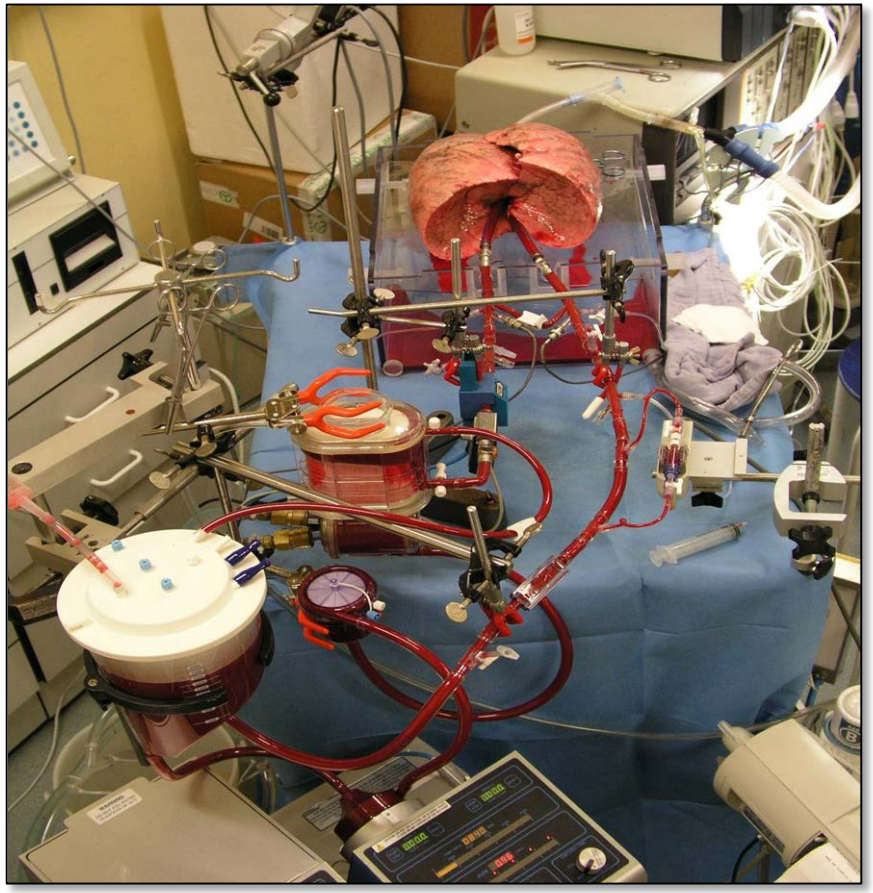
FDA Discussion Question 12 & 13

Clinical Perspectives and Benefit-Risk Assessment

Dirk Van Raemdonck, MD, PhD
Director, Transplant Center
University Hospitals Leuven
Department of Thoracic Surgery

OCS Lung System Provides Necessary Advance to Field of Lung Transplantation

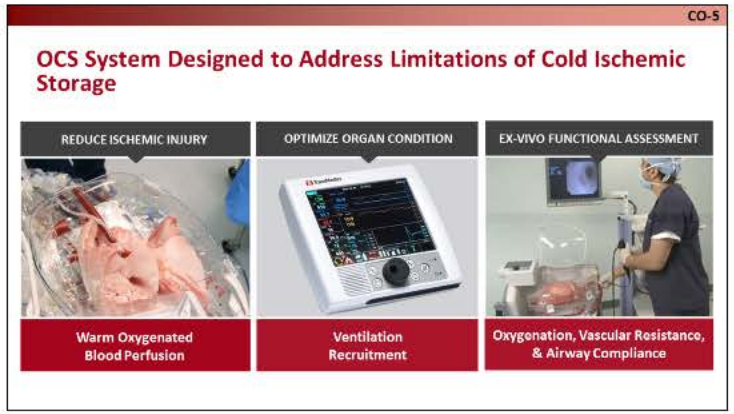
Standard of Care
(1980s)



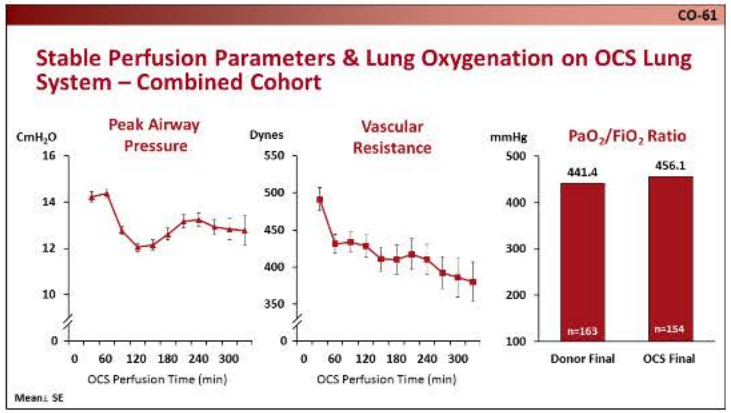
2004

2017

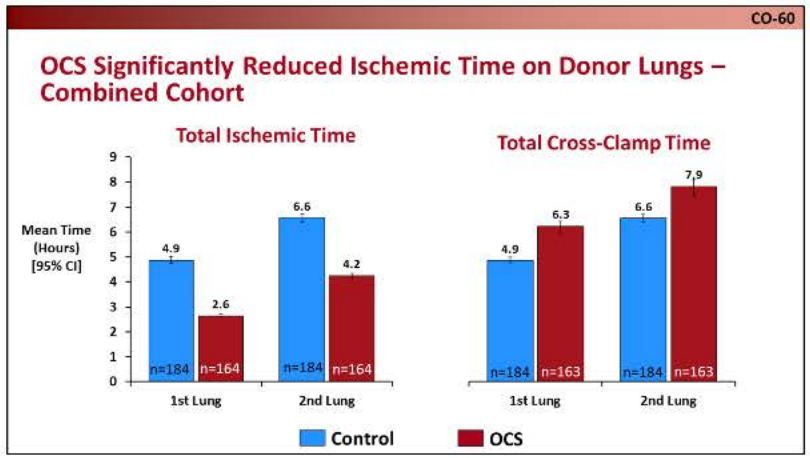
OCS Provides New Optimization and Monitoring Capabilities That are Not Possible with Cold Storage



- Improve quality of donor lung preservation
- Improve clinical decision making

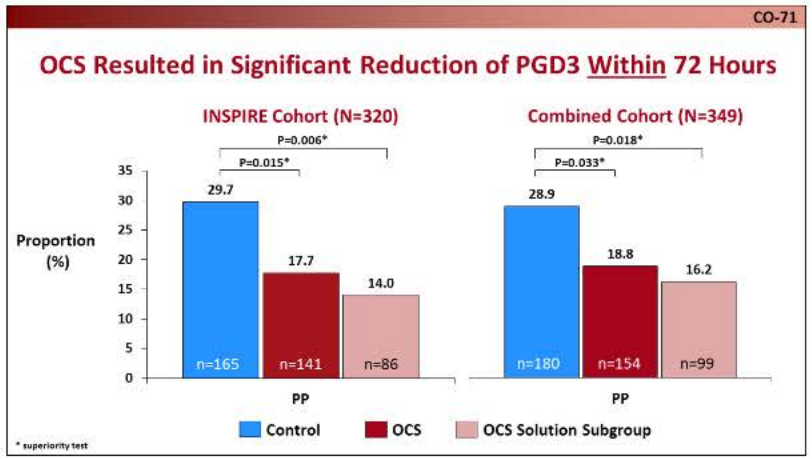


OCS Reduces Ischemic Time on Donor Lungs



- First preservation technology to reduce ischemia on donor lungs
- Ability to travel longer
- Better transplant procedure logistics

OCS First Device To Demonstrate Significant Reduction of Most Severe Form of PGD



- First technology to reduce PGD
- Offers potential for better short- and long-term outcomes
- Encouraging BOS results to be further evaluated post approval

INSPIRE Trial Demonstrates Reasonable Assurance of Safety for OCS Lung System

- Met safety endpoint
- Higher 30-day mortality in OCS was due to non-lung graft related causes
- Overall hospital mortality was similar between arms
- Favorable long-term safety profile with similar survival through 2 years

Effectiveness of OCS Lung System Clearly Demonstrated in INSPIRE Trial

- OCS performed similar to or better than control on most effectiveness measures
- OCS overcomes many limitations of cold storage:
  - Reduces ischemic injury
  - Provides optimization and monitoring capabilities
- Positive benefit-risk profile

OCS Lung Approval Would Enable Future Advancements in Lung Transplantation

- OCS Lung System is a paradigm shift in lung transplantation
- Important first step toward further advancements:
  - Improve long-term viability of donor lungs
  - Increase availability of donor lungs currently wasted due to limitations of cold storage
    - Would reduce mortality on the waiting list
- Providing OCS Lung to patients/physicians in US now critical to advancing field of lung transplantation

TransMedics®

Bringing new life to organ transplantation™

OCS™ Lung System for the Preservation of Donor Lungs for Transplantation

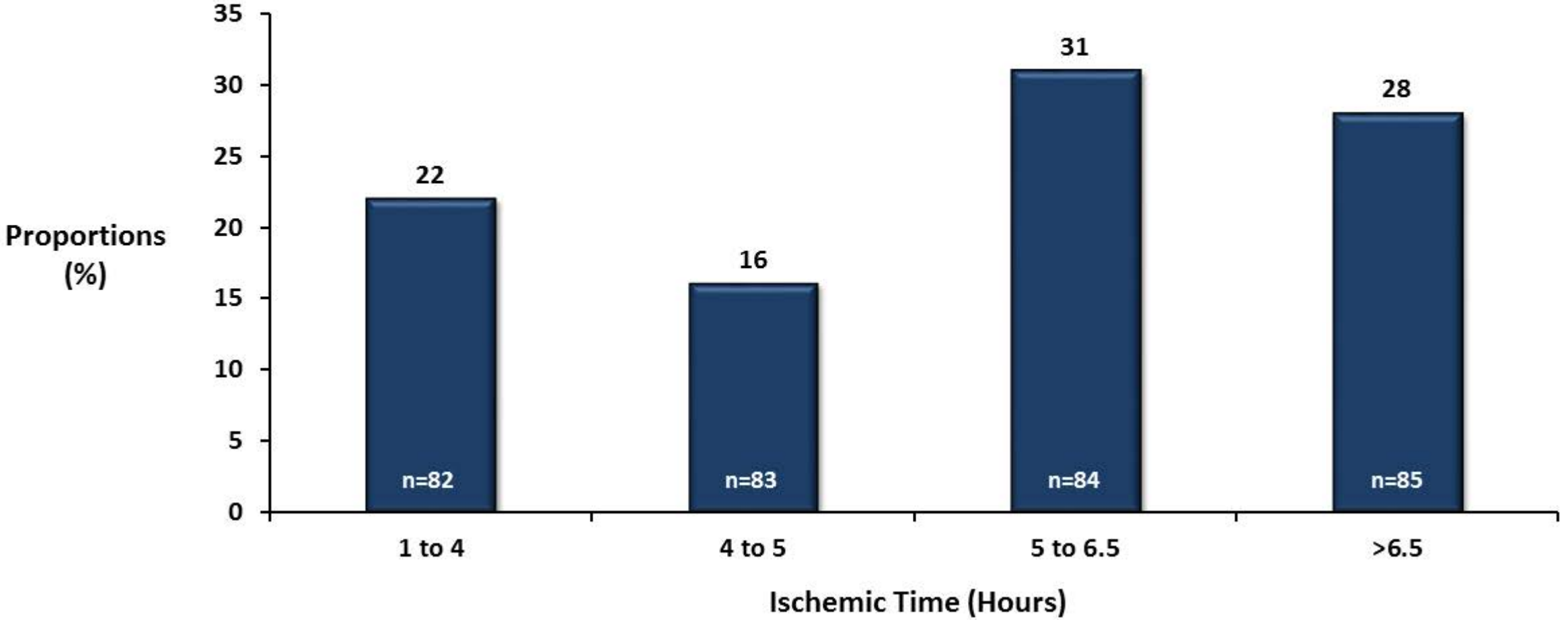
May 17, 2017

TransMedics, Inc.

Gastroenterology-Urology Devices Panel

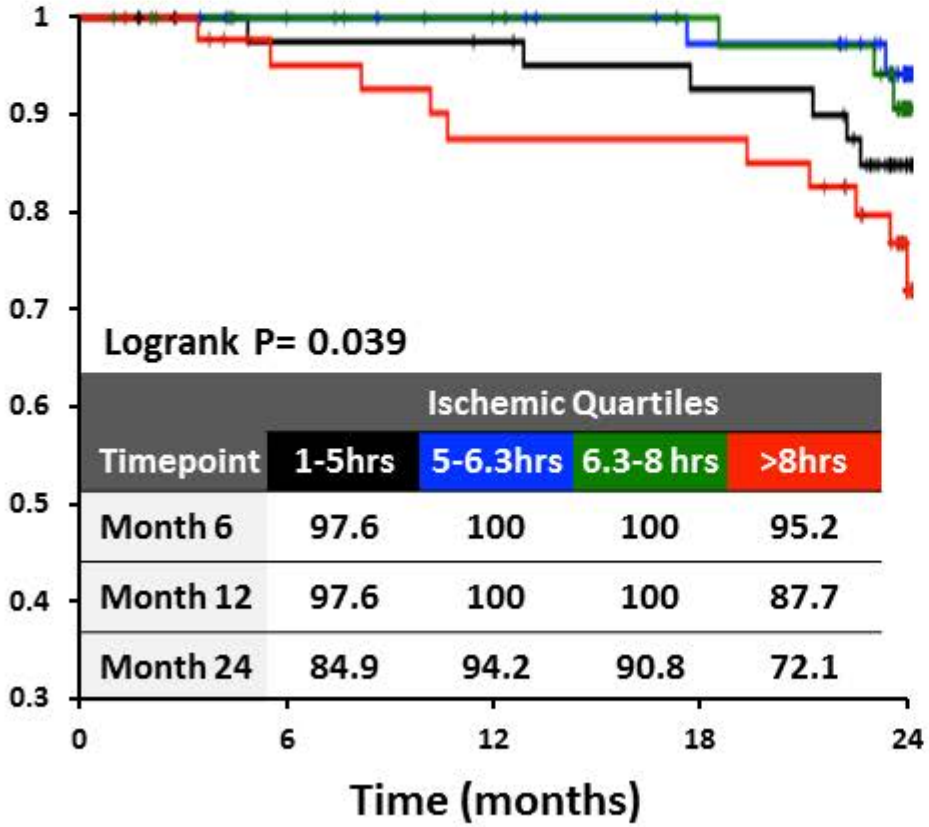
ONSCREEN BACK-UP SLIDES

PGD3 Within 72 Hours Stratified by Ischemic Time Quartiles: Combined Cohort (N=349) – PP Population



BOS-Free Status Through 24 Months by Control Ischemic Quartile Per Protocol Combined Cohort (N=349), Treatment Splits

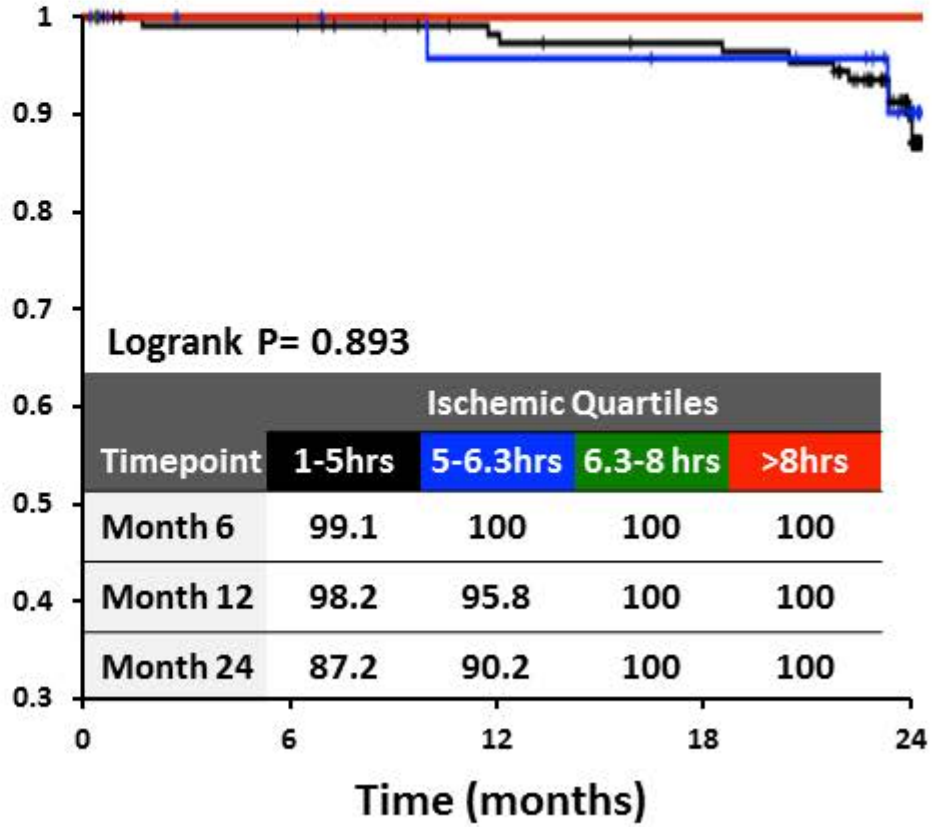
Control



Logrank P= 0.039

Timepoint	Ischemic Quartiles 1-5hrs	5-6.3hrs	6.3-8 hrs	>8hrs
Month 6	97.6	100	100	95.2
Month 12	97.6	100	100	87.7
Month 24	84.9	94.2	90.8	72.1

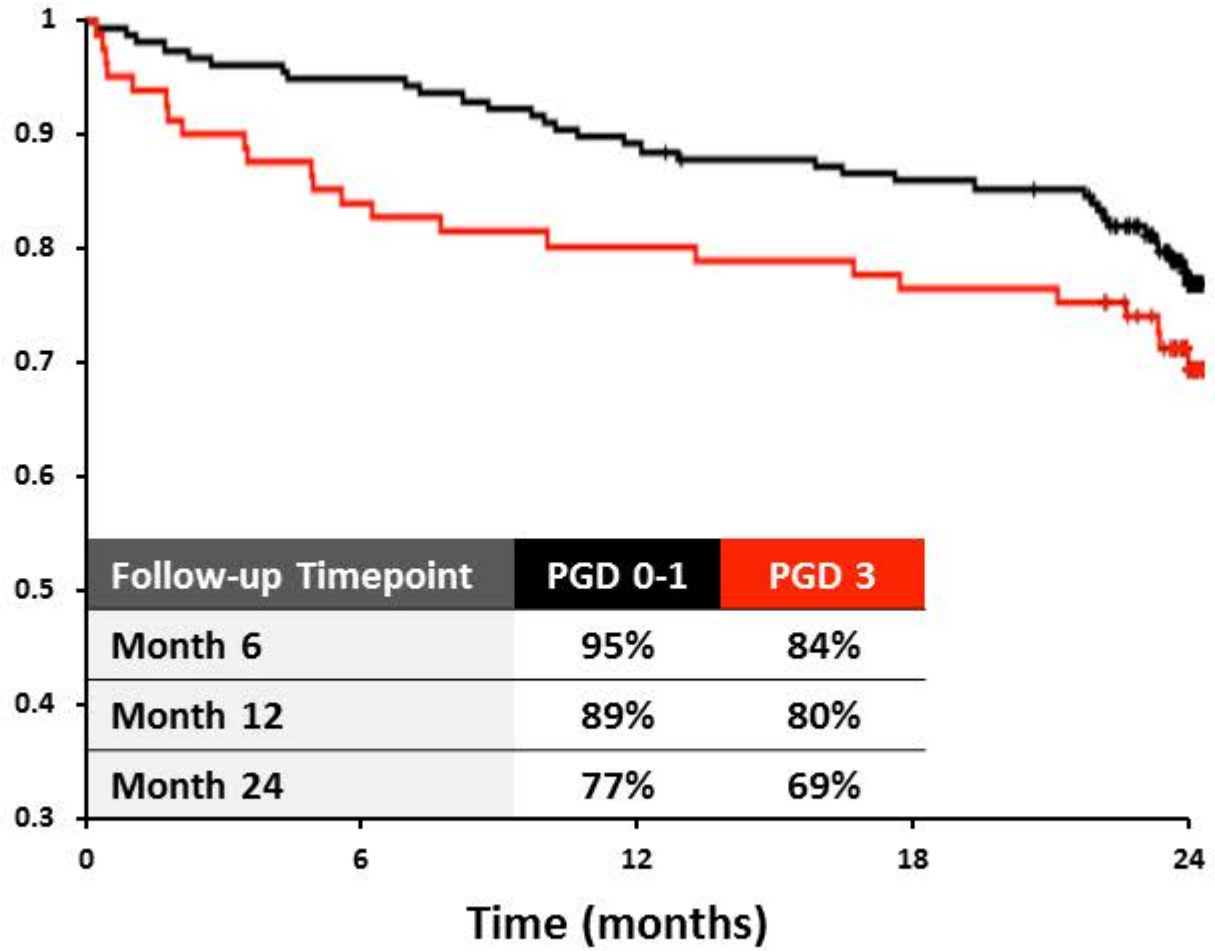
OCS Arm



Logrank P= 0.893

Timepoint	Ischemic Quartiles 1-5hrs	5-6.3hrs	6.3-8 hrs	>8hrs
Month 6	99.1	100	100	100
Month 12	98.2	95.8	100	100
Month 24	87.2	90.2	100	100

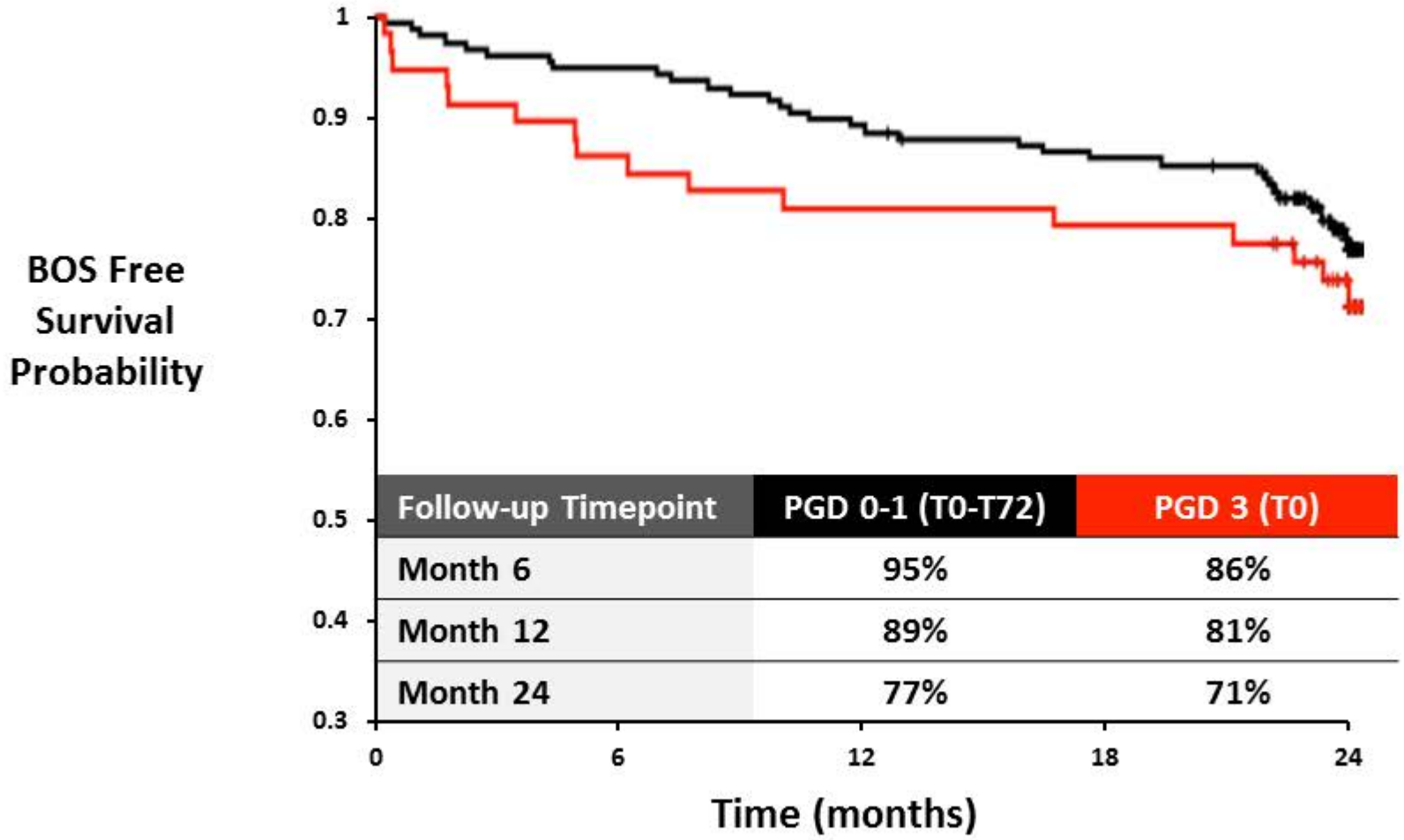
PGD 3 Within 72 Hours and BOS Free Survival Combined Cohort (N=349) – PP



Follow-up Timepoint	PGD 0-1	PGD 3
Month 6	95%	84%
Month 12	89%	80%
Month 24	77%	69%

# at risk					
PGD 0-1	157	149	140	133	66
PGD 3	81	68	65	62	33

PGD 3 at T0 and BOS Free Survival Combined Cohort (N=349) – PP



Follow-up Timepoint	PGD 0-1 (T0-T72)	PGD 3 (T0)
Month 6	95%	86%
Month 12	89%	81%
Month 24	77%	71%

# at risk					
PGD 0-1 in T0-72	157	149	140	133	66
PGD 3 at T0	58	50	47	46	24

Logistics Screen Failure – Transplanted Off Study

At 1st Donor Offer

OCS

- 2 Device was not available for retrieval due to malfunction
- 1 No trained personnel to run OCS

CONTROL

- 1 Randomization envelope not opened prior to retrieval

At 2nd or 3rd Donor Offer

OCS

- 1 pRBCs expired during simultaneous donor offers
- 1 Out of geographical zone donor offer in the UK
- 2 OCS solution used in first donor offer and out of stock
- 3 No trained personnel available to run OCS

Screen Failures

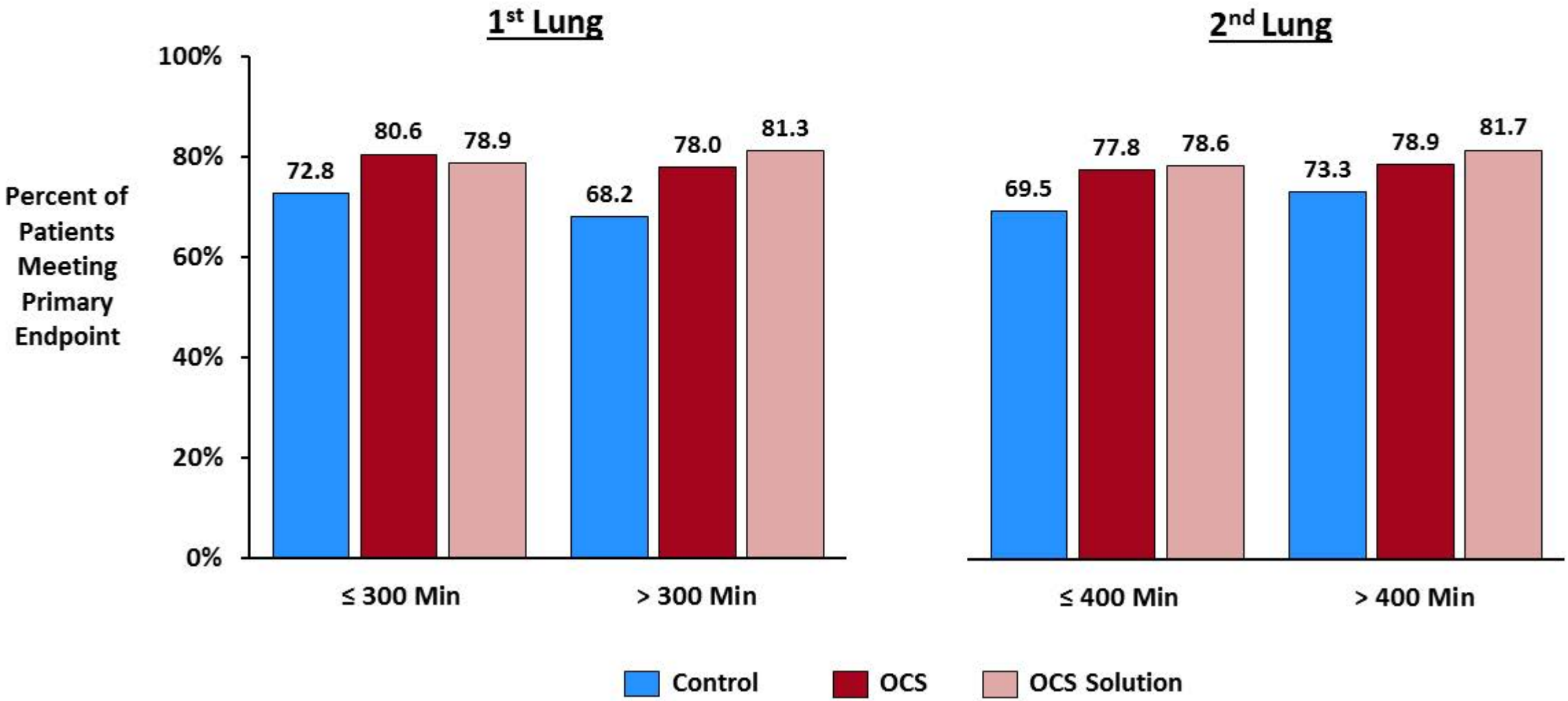
- **mITT Definition**
  - All randomized patients for whom a matching lung has been harvested **and** determined to be eligible for preservation with either Control or OCS before any attempt has been made to preserve the lung with either Control or OCS.
- **Screen Failures not eligible for mITT**
  - Donor lungs turned down for transplant altogether (i.e. “dry runs)
  - Donor lungs harvested but not eligible for INSPIRE according to inclusion/exclusion criteria
  - Donor lungs harvested and eligible for INSPIRE but for which OCS or Control preservation could not be attempted (“Logistics Screen Failures”)
  - Recipient screen failures were subjects who did not meet inclusion/exclusion criteria for INSPIRE at the time that a matching donor lung became available

ITT: N=407
INSPIRE Trial: Pre-Specified Primary Effectiveness Endpoint

	Treatment Difference [Upper 95% CI]
ITT OCS Arm vs. Control	**-3.1% [4.7%]**

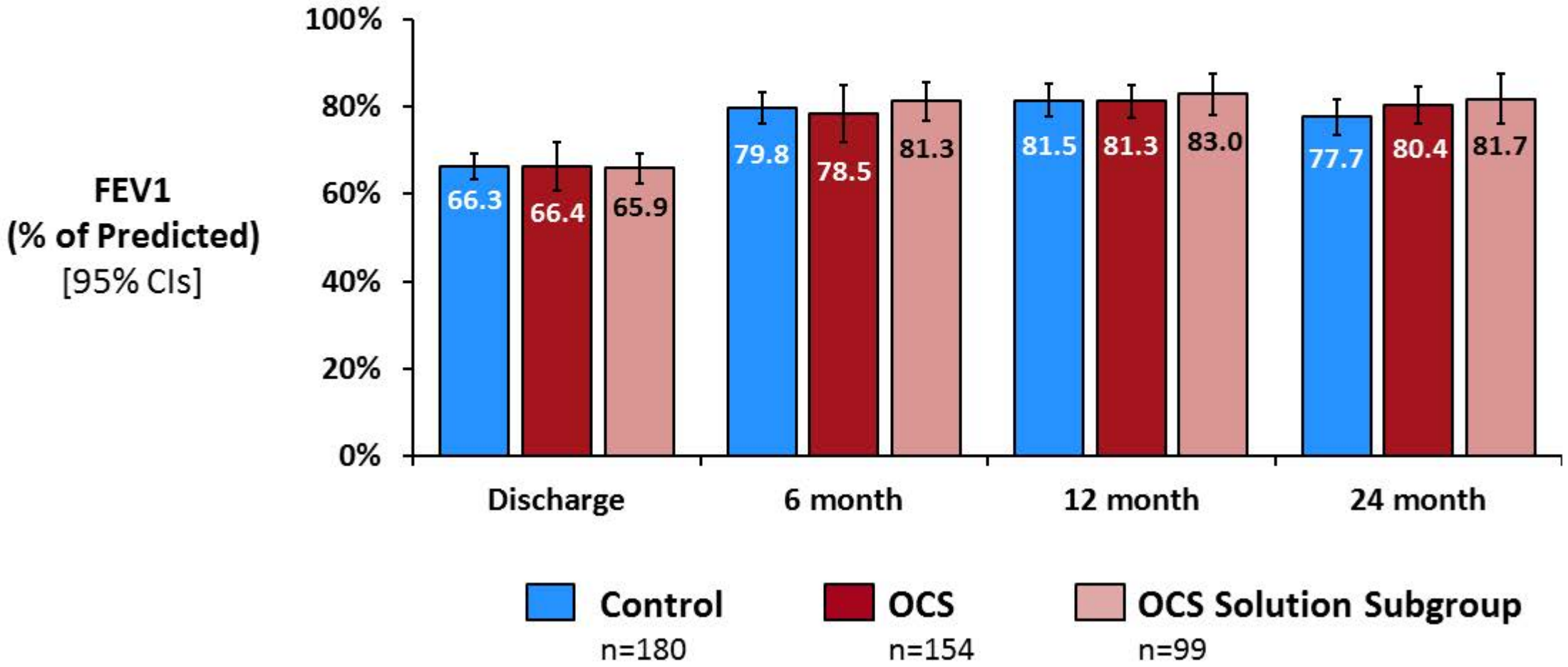
- Imputation Methodology
  - 9 US subjects had known outcomes off-study
  - Multiple imputation without adjustment was used to address unknown outcomes

OCS Performed Better than Control Regardless of Cross-Clamp Time: Combined Cohort (N=349) – PP



Pulmonary Function Test

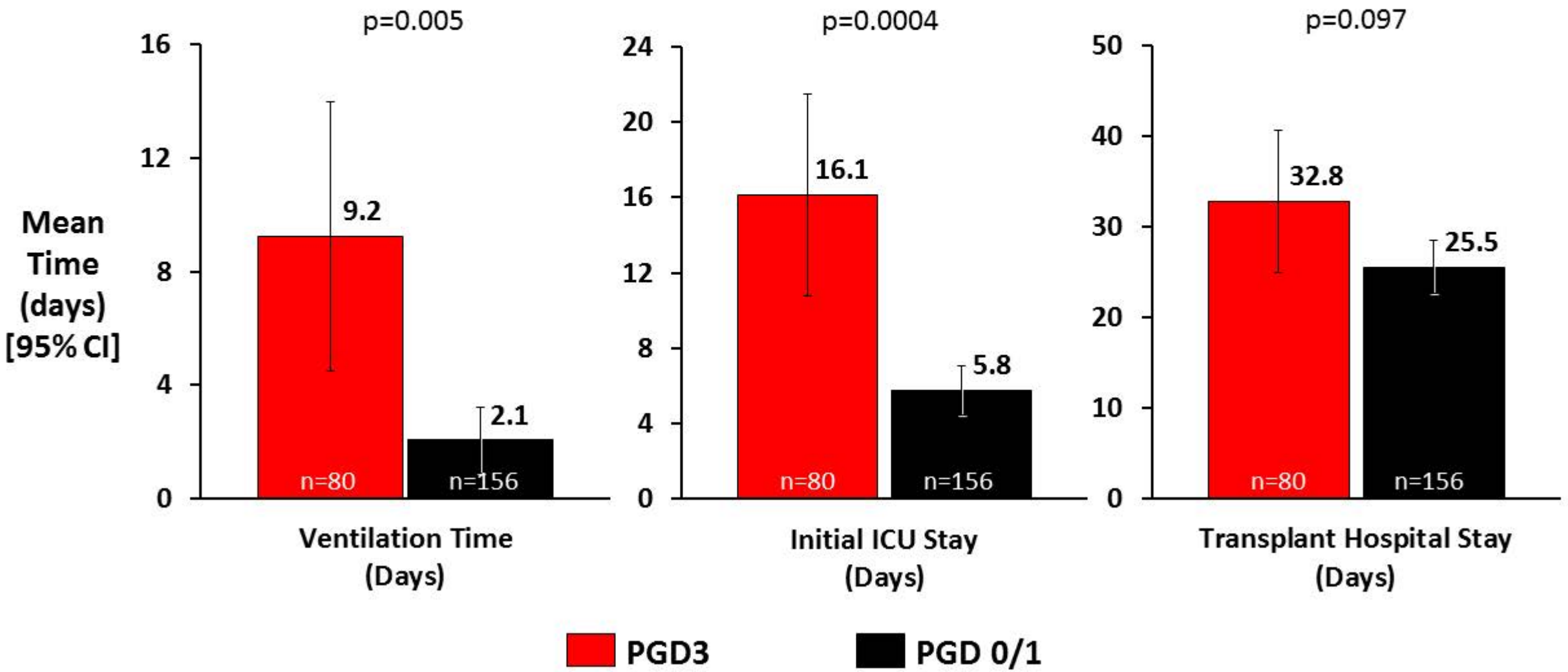
FEV1% Predicted from Discharge Through 24 Months – Combined Cohort (PP)



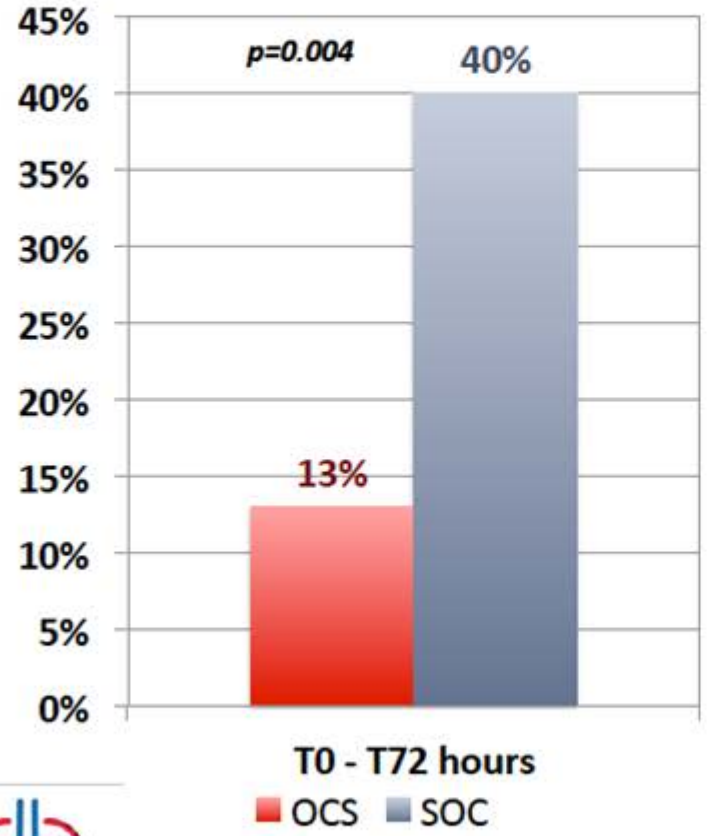
Recipient Characteristics Similar Between Arms

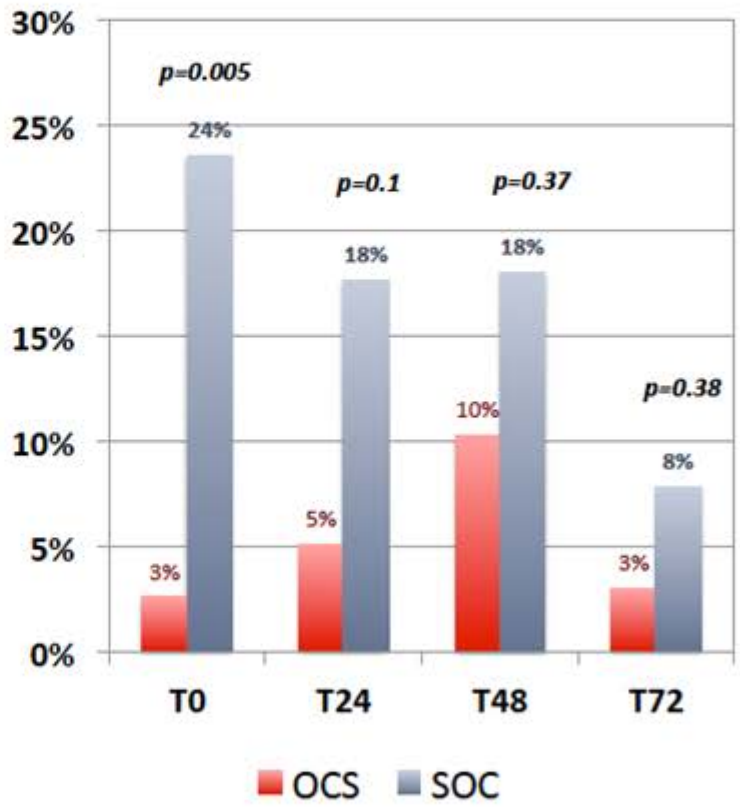
Recipient Characteristic	Control N=184	OCS N=165
Age (years), Mean ± SD	50 ± 14	50 ± 13
Female, %	36%	48%
BMI (kg/m^2), Mean ± SD	23 ± 4.1	23 ± 4.6
LAS Score, Mean ± SD	48 ± 18	51 ± 20
On ECMO on Transplant Day, %	5%	5%
Use of Intraoperative Cardiopulmonary Bypass	38%	40%
Secondary Pulmonary Hypertension, %	32%	40%
Primary Cause of Lung Failure, %		
COPD	28%	28%
IPF	34%	35%
Cystic Fibrosis	23%	21%
IPAH	4%	9%
Sarcoidosis	5%	3%

PGD 3 Within 72 Hours Associated with Significant Increase of Time on Ventilation and ICU Stay – Combined Cohort (N=349) – PP



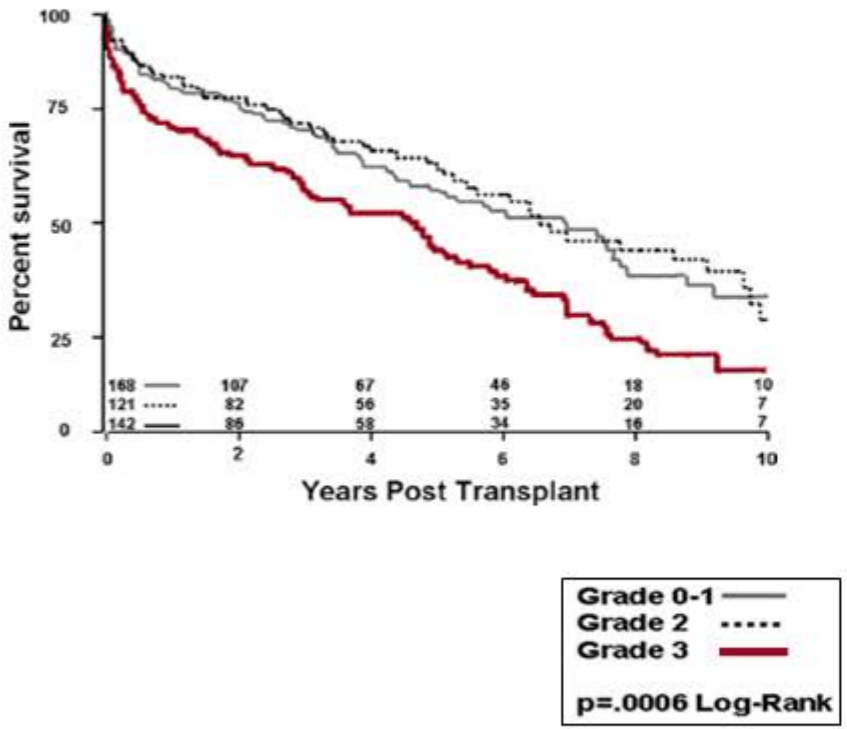
Incidence of Post-Transplant PGD Grade 3





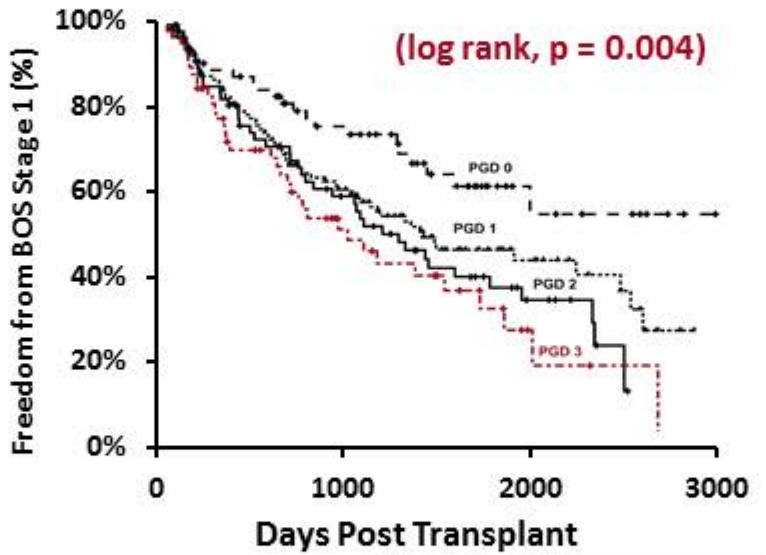
N=90 Subjects

PGD3 Within First 48 Hours Correlates with Lower Long-term Survival, Higher BOS Rate



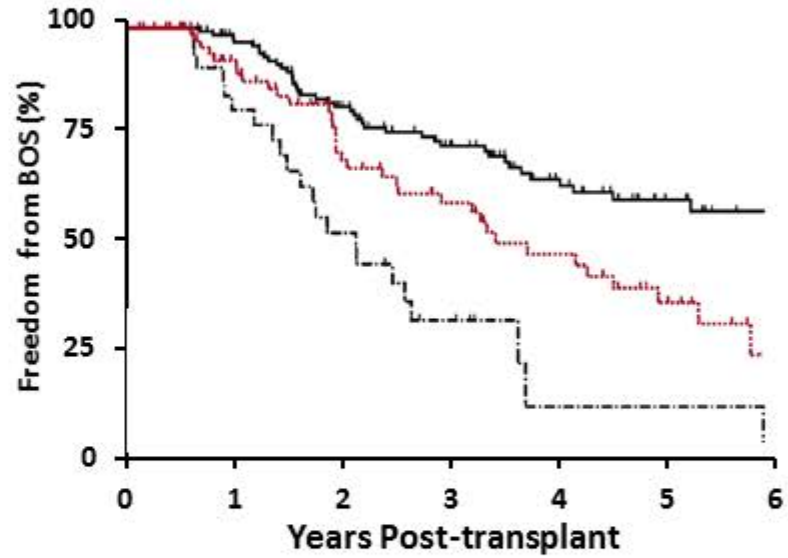
Whitson BA et al., JHLT 2007; 26:1004-1011

PGD 3 at T0 Correlates with Long-Term BOS Rates



Daud et al. AMJ. Resp. & Crit. Care Med. 2007

PGD 2 or 3 at T0 Significant Risk Factor for BOS



HR (95% CI) =2.0 (1.3-3.5) p=0.002 for BOS development

Controls
Transient PGD
PGD2-3 at T0 that improved by T72
Severe PGD

DerHovanessian et al, Am J Transplant. 2016; 16(2): 640–649.

Subject D: Protocol Violation (Ineligible donor lungs due to presence of active pneumonia)

- **Evidence from Site-Entered CRF:**
  - **Eligibility Donor Form**: **Presence of active pulmonary disease**
  - **Donor Assessment Form**: **Pulmonary edema possibly due to aspiration**; ongoing LLL consolidation collapse with focal areas of **left upper lobe "pneumonic infiltrates"**
  - **Donor Lung Assessment Form**: Mucoid/mucopurulent secretions; apical lung scarring

- **FDA's Control Subject Counter Example – Site-Entered CRF**:
  - **Donor Assessment Form**: +++ Polymorphs; ++ RBCs; Yeast isolated; Coagulase negative staphylococcus isolated; Enterobacter cloacae complex isolate
  - **This counter example is not representative of ineligibility, because it only represents upper respiratory flora and not active pneumonia**

Survival by PGD Category

	Survival Probability at 24 Months
PGD 0/1 at all timepoints	87.1%
PGD 3 at T0; PGD 0/1 thereafter	80.0%
PGD 3 at T24; PGD 0/1 thereafter	72.9%
PGD 3 at T48; PGD 0/1 thereafter	83.3%
PGD 3 at 72; PGD 0/1 thereafter	52.5%